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FILE 'HOME' ENTERED AT 16:09:28 ON 15 SEP 2003

=> index bioscience medicine meetings
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.42       0.42

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
       DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 16:10:21 ON 15 SEP 2003

79 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s ((heat (w) shock (w) protein?) or HSP60 or HSP65) and (vascular (w) (disorder? or
disease?) or atherosclos?)
         33   FILE ADISCTI
          1   FILE ADISINSIGHT
        980   FILE BIOSIS
   9 FILES SEARCHED...
          3   FILE BIOTECHABS
          3   FILE BIOTECHDS
         17   FILE BIOTECHNO
          4   FILE CANCERLIT
  14 FILES SEARCHED...
         26   FILE CAPLUS
         45   FILE DDFU
         35   FILE DGENE
  24 FILES SEARCHED...
         48   FILE DRUGU
          2   FILE EMBAL
         40   FILE EMBASE
         11   FILE ESBIOBASE
  33 FILES SEARCHED...
          8   FILE FEDRIP
          1   FILE IFIPAT
        248   FILE JICST-EPLUS
          4   FILE LIFESCI
  44 FILES SEARCHED...
         29   FILE MEDLINE
        413   FILE PASCAL
  51 FILES SEARCHED...
          1   FILE PHIN
          4   FILE PROMT
         29   FILE SCISEARCH
         41   FILE TOXCENTER
        194   FILE USPATFULL
         10   FILE USPAT2
          1   FILE VETU
  65 FILES SEARCHED...
          9   FILE WPIDS
          9   FILE WPINDEX
          7   FILE NLDB
          1   FILE COMPENDEX
  72 FILES SEARCHED...

  31 FILES HAVE ONE OR MORE ANSWERS,   79 FILES SEARCHED IN STNINDEX

L1   QUE ((HEAT (W) SHOCK (W) PROTEIN?) OR HSP60 OR HSP65) AND (VASCULAR (W) (D
       ISORDER? OR DISEASE?) OR ATHEROSCLOS?)
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=> file hits

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.70	8.12

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=> s l1

L2	980	FILE BIOSIS
L3	413	FILE PASCAL
L4	248	FILE JICST-EPLUS
L5	194	FILE USPATFULL
L6	48	FILE DRUGU
L7	41	FILE TOXCENTER
L8	40	FILE EMBASE
L9	35	FILE DGENE
L10	33	FILE ADISCTI
L11	29	FILE MEDLINE
L12	29	FILE SCISEARCH
L13	29	FILE CAPLUS
L14	17	FILE BIOTECHNO
L15	11	FILE ESBIOBASE
L16	10	FILE USPAT2
L17	9	FILE WPIDS
L18	8	FILE FEDRIP
L19	7	FILE NLDB
L20	4	FILE CANCERLIT
L21	4	FILE LIFESCI
L22	4	FILE PROMT
L23	3	FILE BIOTECHDS
L24	2	FILE EMBAL
L25	1	FILE ADISINSIGHT
L26	1	FILE IFIPAT
L27	1	FILE PHIN
L28	1	FILE VETU
L29	1	FILE COMPENDEX

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TOTAL FOR ALL FILES
L30        2203 L1

=> s ((HEAT (W) SHOCK (W) PROTEIN?) OR HSP60 OR HSP65) (s) (VASCULAR (W) (DISORDER? OR
DISEASE?) OR ATHEROSCLOS?)
L31          19 FILE BIOSIS
L32           9 FILE PASCAL
L33           2 FILE JICST-EPLUS
L34          11 FILE USPATFULL
L35           1 FILE DRUGU
L36           5 FILE TOXCENTER
L37          22 FILE EMBASE
L38          27 FILE DGENE
L39           0 FILE ADISCTI
L40           5 FILE MEDLINE
L41          20 FILE SCISEARCH
L42          12 FILE CAPLUS
L43          10 FILE BIOTECHNO
L44          11 FILE ESBIOBASE
L45           0 FILE USPAT2
L46           2 FILE WPIDS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HSP65) (S) '
L47           8 FILE FEDRIP
L48           0 FILE NLDB
L49           4 FILE CANCERLIT
L50           4 FILE LIFESCI
L51           0 FILE PROMT
L52           2 FILE BIOTECHDS
L53           1 FILE EMBAL
L54           0 FILE ADISINSIGHT
L55           0 FILE IFIPAT
L56           0 FILE PHIN
L57           0 FILE VETU
L58           0 FILE COMPENDEX

TOTAL FOR ALL FILES
L59         175 ((HEAT (W) SHOCK (W) PROTEIN?) OR HSP60 OR HSP65) (S) (VASCULAR
                (W) (DISORDER? OR DISEASE?) OR ATHEROSCLOS?)

=> dup rem l59
DUPLICATE IS NOT AVAILABLE IN 'DGENE, FEDRIP, ADISINSIGHT'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L59
L60           90 DUP REM L59 (85 DUPLICATES REMOVED)

=> d l60 1-90 ibib abs

L60  ANSWER 1 OF 90  USPATFULL on STN                    DUPLICATE 1
ACCESSION NUMBER:        2003:112549  USPATFULL
TITLE:                   Methods for treating vascular disease by inhibiting
                         toll-like receptor-4
INVENTOR(S):             Arditi, Moshe, Encino, CA, UNITED STATES
                         Rajavashisth, Tripathi, El Camino Village, CA, UNITED
                         STATES
                         Shah, Prediman K., Los Angeles, CA, UNITED STATES
PATENT ASSIGNEE(S):      CEDARS-SINAI MEDICAL CENTER (U.S. corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2003077279      A1   20030424
APPLICATION INFO.:       US 2002-128166     A1   20020423  (10)

                               NUMBER         DATE
                         ------------------ --------
```

PRIORITY INFORMATION: US 2001-341359P 20011217 (60)
US 2001-335637P 20011024 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pillsbury Winthrop LLP, Intellectual Property Group, Suite 2800, 725 South Figueroa Street, Los Angeles, CA, 90017-5406
NUMBER OF CLAIMS: 60
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods included herein describe the treatment of atherosclerosis and other vascular diseases such as thrombosis, restenosis after angioplasty and/or stenting, and vein-graft disease after bypass surgery, by inhibition of the expression or biologic activity of Toll-like receptor-4 (TLR-4). Also included is an intravascular device coated with a compound that inhibits TLR-4; thereby imparting an improved efficacy to the device. TLR-4 cell signal transduction is at least partially responsible for the manifestation, continuation, and/or worsening of atherosclerosis and other forms of vascular disease. The present invention provides several means with which to inhibit this signal transduction pathway.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 2 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:214343 USPATFULL
TITLE: Methods for treating vascular disease by inhibiting myeloid differentiation factor 88
INVENTOR(S): Arditi, Moshe, Encino, CA, UNITED STATES
Rajavashisth, Tripathi, El Camino Village, CA, UNITED STATES
Shah, Prediman K., Los Angeles, CA, UNITED STATES
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, Los Angeles, CA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003148986	A1	20030807
APPLICATION INFO.:	US 2002-317992	A1	20021212 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-128166, filed on 23 Apr 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-341359P	20011217 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Richard H. Zaitlen, Esq., Pillsbury Winthrop LLP, Intellectual Property Group, 725 South Figueroa Street, Suite 2800, Los Angeles, CA, 90017-5406
NUMBER OF CLAIMS: 56
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1237
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods included herein describe the treatment of atherosclerosis and other vascular diseases such as thrombosis, restenosis after angioplasty and/or stenting, and vein-graft disease after bypass surgery, by inhibition of the expression or biologic activity of myeloid differentiation factor 88 (MyD88). Also included is an intravascular device coated with a compound that inhibits MyD88; thereby imparting an improved efficacy to the device. TLR-4 cell signal transduction is at least partially responsible for the manifestation, continuation, and/or

worsening of atherosclerosis and other forms of vascular disease. The present invention provides several means with which to inhibit this signal transduction pathway by affecting the biological activity of MyD88.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 3 OF 90 USPATFULL on STN

ACCESSION NUMBER: 2003:200905 USPATFULL

TITLE: Novel G protein-coupled receptor family members, human thioredoxin family members, human leucine-rich repeat family members, and human ringfinger family member

INVENTOR(S): Glucksmann, Maria Alexandra, Lexington, MA, UNITED STATES
Silos-Santiago, Inmaculada, Jamaica Plain, MA, UNITED STATES
Galvin, Katherine M., Jamaica Plain, MA, UNITED STATES
Weich, Nadine, Brookline, MA, UNITED STATES
Curtis, Rory A. J., Framingham, MA, UNITED STATES
Bandaru, Rajasekhar, Watertown, MA, UNITED STATES
Kapeller-Libermann, Rosana, Chestnut Hill, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003138890	A1	20030724
APPLICATION INFO.:	US 2002-145586	A1	20020514 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-796338, filed on 28 Feb 2001, PENDING Continuation-in-part of Ser. No. WO 2001-US6543, filed on 28 Feb 2001, PENDING

PRIORITY INFORMATION:	NUMBER	DATE
	WO 2001-US6057	20010223
	WO 2001-US23152	20010723
	WO 2001-US40476	20010409
	WO 2001-US7139	20010305
	WO 2001-US19544	20010615
	WO 2001-US29967	20010925
	WO 2001-US9470	20010323
	WO 2001-US10380	20010330
	WO 2001-US29968	20010925
	US 2000-186059P	20000229 (60)
	US 2000-220042P	20000721 (60)
	US 2000-187447P	20000307 (60)
	US 2000-211673P	20000615 (60)
	US 2000-235049P	20000925 (60)
	US 2000-191863P	20000324 (60)
	US 2000-193919P	20000331 (60)
	US 2000-235032P	20000925 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JOHN W. FREEMAN, ESQ., Fish & Richardson P.C., 225 Franklin Street, Boston, MA, 02110-2804
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 97 Drawing Page(s)
LINE COUNT: 51652
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides isolated nucleic acids molecules, designated 20716, 65494, 44576, 1983, 52881, 2398, 45449, 50289, 52872, 22105, 22109, 22108, 47916, 33395, 31939, and 84241 nucleic acid molecules, which encode novel G protein-coupled receptor family members, human thioredoxin family members, human leucine-rich repeat family members, and human ringfinger family member. The invention also provides

antisense nucleic acid molecules, recombinant expression vectors containing 20716, 65494, 44576, 1983, 52881, 2398, 45449, 50289, 52872, 22105, 22109, 22108, 47916, 33395, 31939, or 84241 nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a 20716, 65494, 44576, 1983, 52881, 2398, 45449, 50289, 52872, 22105, 22109, 22108, 47916, 33395, 31939, or 84241 gene has been introduced or disrupted. The invention still further provides isolated 20716, 65494, 44576, 1983, 52881, 2398, 45449, 50289, 52872, 22105, 22109, 22108, 47916, 33395, 31939, or 84241 proteins, fusion proteins, antigenic peptides and anti-20716, 65494, 44576, 1983, 52881, 2398, 45449, 50289, 52872, 22105, 22109, 22108, 47916, 33395, 31939, or 84241 antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 4 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:146290 USPATFULL
TITLE: Saliva immunoassay for detection of antibodies for cardiovascular disease
INVENTOR(S): Vojdani, Aristo, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003100036	A1	20030529	
APPLICATION INFO.:	US 2001-5710	A1	20011108	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for diagnosing the likelihood and severity of cardiovascular disease in a patient is disclosed. The method determines the levels of antibodies against autoantigens, including myosin, oxidized LDL, .beta.-2-glycoprotein, heat shock protein-60, platelet glycoprotein, and immune complexes. It then compares the results to normal levels to determine the likelihood and severity of cardiovascular disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 5 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:146289 USPATFULL
TITLE: Saliva immunoassay for detection of antibodies for autoimmune disease
INVENTOR(S): Vojdani, Aristo, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003100035	A1	20030529	
APPLICATION INFO.:	US 2001-5684	A1	20011108	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 923
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for diagnosing the likelihood and severity of autoimmune disease in a patient is disclosed. The method determines the levels of

antibodies against autoantigens, including lupus peptide, arthritis peptide, platelet glycoprotein, and immune complexes. It then compares the results to normal levels to determine the likelihood and severity of the autoimmune disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 6 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:146184 USPATFULL
TITLE: Saliva immunoassay for detection of exposure to infectious agents
INVENTOR(S): Vojdani, Aristo, Los Angeles, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003099929	A1	20030529
APPLICATION INFO.:	US 2001-7768	A1	20011108 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for diagnosing the exposure to infectious agents in a patient is disclosed. The method determines the levels of antibodies against infectious agents, including bacterial, parasitic, and viral agents. It then compares the results to normal levels to determine the exposure to infectious agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 7 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:134804 USPATFULL
TITLE: Secreted protein HEMAE80
INVENTOR(S): Young, Paul, Gaithersburg, MD, UNITED STATES
Greene, John M., Gaithersburg, MD, UNITED STATES
Ferrie, Ann M., Painted Post, NY, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Rosen, Craig A., Laytonsville, MD, UNITED STATES
Hu, Jing-Shan, Mountain View, CA, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Brewer, Laurie A., St. Paul, MN, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
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Florence, Charles, Rockville, MD, UNITED STATES
Florence, Kimberly, Rockville, MD, UNITED STATES
Lafleur, David W., Washington, DC, UNITED STATES
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Fan, Ping, Potomac, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Fischer, Carrie L., Burke, VA, UNITED STATES
Soppet, Daniel R., Centerville, VA, UNITED STATES
Li, Yi, Sunnyvale, CA, UNITED STATES
Zeng, Zhizhen, Lansdale, PA, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES
Yu, Guo-Liang, Berkeley, CA, UNITED STATES
Feng, Ping, Gaithersburg, MD, UNITED STATES
Dillon, Patrick J., Carlsbad, CA, UNITED STATES
Endress, Gregory A., Florence, MA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., Rockville, MD, UNITED

STATES, 20850 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003092893	A1	20030515
APPLICATION INFO.:	US 2001-23282	A1	20011220 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-205258, filed on 4 Dec 1998, PENDING Continuation-in-part of Ser. No. WO 1998-US11422, filed on 4 Jun 1998, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-48885P	19970606 (60)
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	US 1997-48881P	19970606 (60)
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US 1998-92921P	19980715	(60)
US 1998-94657P	19980730	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
NUMBER OF CLAIMS: 75
EXEMPLARY CLAIM: 1
LINE COUNT: 17991
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 8 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:93799 USPATFULL
TITLE: Secreted protein HEMAE80
INVENTOR(S): Young, Paul, Gaithersburg, MD, UNITED STATES
Greene, John M., Gaithersburg, MD, UNITED STATES
Ferrie, Ann M., Painted Post, NY, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Rosen, Craig A., Laytonsville, MD, UNITED STATES
Hu, Jing-Shan, Mountain View, CA, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
Brewer, Laurie A., St. Paul, MN, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Florence, Charles, Rockville, MD, UNITED STATES
Florence, Kimberly, Rockville, MD, UNITED STATES
Lafleur, David W., Washington, DC, UNITED STATES
Ni, Jian, Germantown, MD, UNITED STATES
Fan, Ping, Potomac, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Fischer, Carrie L., Burke, VA, UNITED STATES
Soppet, Daniel R., Centerville, VA, UNITED STATES
Li, Yi, Sunnyvale, CA, UNITED STATES
Zeng, Zhizhen, lansdale, PA, UNITED STATES
Kyaw, Hla, Frederick, MD, UNITED STATES

Yu, Guo-Liang, Berkeley, CA, UNITED STATES
Feng, Ping, Gaithersburg, MD, UNITED STATES
Dillon, Patrick J., Carlsbad, CA, UNITED STATES
Endress, Gregory A., Florence, MA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003065160	A1	20030403
APPLICATION INFO.:	US 2001-4860	A1	20011207 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-205258, filed on 4 Dec 1998, PENDING Continuation-in-part of Ser. No. WO 1998-US11422, filed on 4 Jun 1998, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-48885P	19970606 (60)
	US 1997-49375P	19970606 (60)
	US 1997-48881P	19970606 (60)
	US 1997-48880P	19970606 (60)
	US 1997-48896P	19970606 (60)
	US 1997-49020P	19970606 (60)
	US 1997-48876P	19970606 (60)
	US 1997-48895P	19970606 (60)
	US 1997-48884P	19970606 (60)
	US 1997-48894P	19970606 (60)
	US 1997-48971P	19970606 (60)
	US 1997-48964P	19970606 (60)
	US 1997-48882P	19970606 (60)
	US 1997-48899P	19970606 (60)
	US 1997-48893P	19970606 (60)
	US 1997-48900P	19970606 (60)
	US 1997-48901P	19970606 (60)
	US 1997-48892P	19970606 (60)
	US 1997-48915P	19970606 (60)
	US 1997-49019P	19970606 (60)
	US 1997-48970P	19970606 (60)
	US 1997-48972P	19970606 (60)
	US 1997-48916P	19970606 (60)
	US 1997-49373P	19970606 (60)
	US 1997-48875P	19970606 (60)
	US 1997-49374P	19970606 (60)
	US 1997-48917P	19970606 (60)
	US 1997-48949P	19970606 (60)
	US 1997-48974P	19970606 (60)
	US 1997-48883P	19970606 (60)
	US 1997-48897P	19970606 (60)
	US 1997-48898P	19970606 (60)
	US 1997-48962P	19970606 (60)
	US 1997-48963P	19970606 (60)
	US 1997-48877P	19970606 (60)
	US 1997-48878P	19970606 (60)
	US 1997-57645P	19970905 (60)
	US 1997-57642P	19970905 (60)
	US 1997-57668P	19970905 (60)
	US 1997-57635P	19970905 (60)
	US 1997-57627P	19970905 (60)
	US 1997-57667P	19970905 (60)
	US 1997-57666P	19970905 (60)
	US 1997-57764P	19970905 (60)
	US 1997-57643P	19970905 (60)
	US 1997-57769P	19970905 (60)
	US 1997-57763P	19970905 (60)

US 1997-57650P	19970905	(60)
US 1997-57584P	19970905	(60)
US 1997-57647P	19970905	(60)
US 1997-57661P	19970905	(60)
US 1997-57662P	19970905	(60)
US 1997-57646P	19970905	(60)
US 1997-57654P	19970905	(60)
US 1997-57651P	19970905	(60)
US 1997-57644P	19970905	(60)
US 1997-57765P	19970905	(60)
US 1997-57762P	19970905	(60)
US 1997-57775P	19970905	(60)
US 1997-57648P	19970905	(60)
US 1997-57774P	19970905	(60)
US 1997-57649P	19970905	(60)
US 1997-57770P	19970905	(60)
US 1997-57771P	19970905	(60)
US 1997-57761P	19970905	(60)
US 1997-57760P	19970905	(60)
US 1997-57776P	19970905	(60)
US 1997-57778P	19970905	(60)
US 1997-57629P	19970905	(60)
US 1997-57628P	19970905	(60)
US 1997-57777P	19970905	(60)
US 1997-57634P	19970905	(60)
US 1997-70923P	19971218	(60)
US 1998-92921P	19980715	(60)
US 1998-94657P	19980730	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
NUMBER OF CLAIMS: 52
EXEMPLARY CLAIM: 1
LINE COUNT: 17645
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 9 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:86313 USPATFULL
TITLE: Novel human 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 molecules and uses therefor
INVENTOR(S): Meyers, Rachel E., Newton, MA, UNITED STATES
Rudolph-Owen, Laura A., Jamaica Plain, MA, UNITED STATES
Kapeller-Libermann, Rosana, Chestnut Hill, MA, UNITED STATES
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., Cambridge, MA, UNITED STATES, 02139 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003059919	A1	20030327
APPLICATION INFO.:	US 2002-160501	A1	20020530 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-838573, filed on 18 Apr 2001, PENDING Continuation-in-part of Ser.

No. US 2001-870133, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870130, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-862535, filed on 21 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870383, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-860821, filed on 18 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-870110, filed on 29 May 2001, PENDING Continuation-in-part of Ser. No. US 2001-907509, filed on 16 Jul 2001, PENDING Continuation-in-part of Ser. No. US 2001-945327, filed on 31 Aug 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-197747P	20000418 (60)
	US 2000-207649P	20000526 (60)
	US 2000-207640P	20000526 (60)
	US 2000-205961P	20000519 (60)
	US 2000-207506P	20000526 (60)
	US 2000-205449P	20000519 (60)
	US 2000-207650P	20000526 (60)
	US 2000-218385P	20000714 (60)
	US 2000-229425P	20000831 (60)
	US 2001-318581P	20010910 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 100 Drawing Page(s)
LINE COUNT: 44311
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides isolated nucleic acids molecules, designated 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 nucleic acid molecules, which encode novel GTPase activating molecules, cadherin molecules, and ankyrin containing family members. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 nucleic acid molecules, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, or 48118 gene has been introduced or disrupted. The invention still further provides isolated 39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 polypeptides, fusion polypeptides, antigenic peptides and anti-39228, 21956, 25856, 22244, 8701, 32263, 50250, 55158, 47765, 62088, 50566, and 48118 antibodies. Diagnostic and therapeutic methods utilizing compositions of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 10 OF 90 USPATFULL on STN
ACCESSION NUMBER: 2003:53885 USPATFULL
TITLE: Precerebellin-like protein
INVENTOR(S): Young, Paul, Gaithersburg, MD, United States
Greene, John M., Gaithersburg, MD, United States
Ferrie, Ann M., Tewksbury, MA, United States
Ruben, Steven M., Olney, MD, United States
Rosen, Craig A., Laytonsville, MD, United States
Hu, Jing-Shan, Sunnyvale, CA, United States
Olsen, Henrik S., Gaithersburg, MD, United States
Ebner, Reinhard, Gaithersburg, MD, United States
Brewer, Laurie A., St. Paul, MN, United States

Moore, Paul A., Germantown, MD, United States
Shi, Yanggu, Gaithersburg, MD, United States
Florence, Charles, Rockville, MD, United States
Florence, Kimberly, Rockville, MD, United States
Lafleur, David W., Washington, DC, United States
Ni, Jian, Rockville, MD, United States
Fan, Ping, Gaithersburg, MD, United States
Wei, Ying-Fei, Berkeley, CA, United States
Fischer, Carrie L., Burke, VA, United States
Soppet, Daniel R., Centreville, VA, United States
Li, Yi, Sunnyvale, CA, United States
Zeng, Zhizhen, Gaithersburg, MD, United States
Kyaw, Hla, Frederick, MD, United States
Yu, Guo-Liang, Berkeley, CA, United States
Feng, Ping, Gaithersburg, MD, United States
Dillon, Patrick J., Carlsbad, CA, United States
Endress, Gregory A., Potomac, MD, United States
Carter, Kenneth C., North Potomac, MD, United States

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6525174	B1	20030225
APPLICATION INFO.:	US 1998-205258		19981204 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1998-US11422, filed on 4 Jun 1998

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-70923P	19971218 (60)
	US 1998-94657P	19980730 (60)
	US 1997-48885P	19970606 (60)
	US 1997-49375P	19970606 (60)
	US 1997-48881P	19970606 (60)
	US 1997-48880P	19970606 (60)
	US 1997-48896P	19970606 (60)
	US 1997-49020P	19970606 (60)
	US 1997-48876P	19970606 (60)
	US 1997-48895P	19970606 (60)
	US 1997-48884P	19970606 (60)
	US 1997-48894P	19970606 (60)
	US 1997-48971P	19970606 (60)
	US 1997-48964P	19970606 (60)
	US 1997-48882P	19970606 (60)
	US 1997-48899P	19970606 (60)
	US 1997-48893P	19970606 (60)
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	US 1997-48901P	19970606 (60)
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	US 1997-49019P	19970606 (60)
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	US 1997-48875P	19970606 (60)
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	US 1997-48917P	19970606 (60)
	US 1997-48949P	19970606 (60)
	US 1997-48974P	19970606 (60)
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	US 1997-48897P	19970606 (60)
	US 1997-48898P	19970606 (60)
	US 1997-48962P	19970606 (60)

US 1997-48963P	19970606	(60)
US 1997-48877P	19970606	(60)
US 1997-48878P	19970606	(60)
US 1997-57645P	19970905	(60)
US 1997-57642P	19970905	(60)
US 1997-57668P	19970905	(60)
US 1997-57635P	19970905	(60)
US 1997-57627P	19970905	(60)
US 1997-57667P	19970905	(60)
US 1997-57666P	19970905	(60)
US 1997-57764P	19970905	(60)
US 1997-57643P	19970905	(60)
US 1997-57769P	19970905	(60)
US 1997-57763P	19970905	(60)
US 1997-57650P	19970905	(60)
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US 1997-57765P	19970905	(60)
US 1997-57762P	19970905	(60)
US 1997-57775P	19970905	(60)
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US 1997-57776P	19970905	(60)
US 1997-57778P	19970905	(60)
US 1997-57629P	19970905	(60)
US 1997-57628P	19970905	(60)
US 1997-57777P	19970905	(60)
US 1997-57634P	19970905	(60)
US 1997-70923P	19971218	(60)
US 1998-92921	19980715	(09)
US 1998-94657P	19980730	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Brusca, John S.
ASSISTANT EXAMINER: Moran, Marjorie A.
LEGAL REPRESENTATIVE: Human Genome Sciences, Inc.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 16937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 11 OF 90 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:373862 CAPLUS
DOCUMENT NUMBER: 138:380364

TITLE: A nucleic acid array of genes associated with disease responses in macrophages and their use in the diagnosis of disease
INVENTOR(S): Stuhlmueller, Bruno; Haeupl, Thomas
PATENT ASSIGNEE(S): Oligene G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1310567	A2	20030514	EP 2002-90348	20021002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
DE 10155600	A1	20030522	DE 2001-10155600	20011109

PRIORITY APPLN. INFO.: DE 2001-10155600 A 20011109
AB An array of .apprxeq.250 genes that show differential expression in macrophages in health and immune disorders is described for use in the diagnosis and monitoring of macrophage assocd. immune disorders and in screening of drugs.

L60 ANSWER 12 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
ACCESSION NUMBER: 2003:420733 BIOSIS
DOCUMENT NUMBER: PREV200300420733
TITLE: Novel complexes of guanylate cyclase with heat shock protein 90 and nitric oxide synthase.
AUTHOR(S): Venema, Richard C.; Venema, Virginia J.; Ju, Hong; Harris, M. Brennan; Snead, Connie; Jilling, Tamas; Dimitropoulou, Christiana; Maragoudakis, Michael E.; Catravas, John D. (1)
CORPORATE SOURCE: (1) Vascular Biology Center, Medical College of Georgia, Augusta, GA, 30912-2500, USA: jcatrava@mail.mcg.edu USA
SOURCE: American Journal of Physiology, (August 2003, 2003) Vol. 285, No. 2 Part 2, pp. H669-H678. print.
ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Soluble guanylate cyclase (sGC) is an important downstream intracellular target of nitric oxide (NO) that is produced by endothelial NO synthase (eNOS) and inducible NO synthase (iNOS). In this study, we demonstrate that sGC exists in a complex with eNOS and **heat shock protein** 90 (HSP90) in aortic endothelial cells. In addition, we show that in aortic smooth muscle cells, sGC forms a complex with HSP90. Formation of the sGC/eNOS/HSP90 complex is increased in response to eNOS-activating agonists in a manner that depends on HSP90 activity. In vitro binding assays with glutathione S-transferase fusion proteins that contain the alpha- or beta-subunit of sGC show that the sGC beta-subunit interacts directly with HSP90 and indirectly with eNOS. Confocal immunofluorescent studies confirm the subcellular colocalization of sGC and HSP90 in both endothelial and smooth muscle cells. Complex formation of sGC with HSP90 facilitates responses to NO donors in cultured cells (cGMP accumulation) as well as in anesthetized rats (hypotension). These complexes likely function to stabilize sGC as well as to provide directed intracellular transfer of NO from NOS to sGC, thus preventing inactivation of NO by superoxide anion and formation of peroxynitrite, which is a toxic molecule that has been implicated in the pathology of several **vascular diseases**.

L60 ANSWER 13 OF 90 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2003:36885899 BIOTECHNO
TITLE: Novel complexes of guanylate cyclase with heat shock

protein 90 and nitric oxide synthase

AUTHOR: Venema R.C.; Venema V.J.; Ju H.; Harris M.B.; Snead C.; Jilling T.; Dimitropoulou C.; Maragoudakis M.E.; Catravas J.D.

CORPORATE SOURCE: J.D. Catravas, Vascular Biology Center, Medical College of Georgia, Augusta, GA 30912-2500, United States.
E-mail: jcatrava@mail.mcg.edu

SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (01 AUG 2003), 285/2 54-2 (H669-H678), 30 reference(s)
CODEN: AJPPDI ISSN: 0363-6135

DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2003:36885899 BIOTECHNO

AB Soluble guanylate cyclase (sGC) is an important downstream intracellular target of nitric oxide (NO) that is produced by endothelial NO synthase (eNOS) and inducible NO synthase (iNOS). In this study, we demonstrate that sGC exists in a complex with eNOS and **heat shock protein** 90 (HSP90) in aortic endothelial cells. In addition, we show that in aortic smooth muscle cells, sGC forms a complex with HSP90. Formation of the sGC/eNOS/HSP90 complex is increased in response to eNOS-activating agonists in a manner that depends on HSP90 activity. In vitro binding assays with glutathione S-transferase fusion proteins that contain the .alpha.- or .beta.-subunit of sGC show that the sGC .beta.-subunit interacts directly with HSP90 and indirectly with eNOS. Confocal immunofluorescent studies confirm the subcellular colocalization of sGC and HSP90 in both endothelial and smooth muscle cells. Complex formation of sGC with HSP90 facilitates responses to NO donors in cultured cells (cGMP accumulation) as well as in anesthetized rats (hypotension). These complexes likely function to stabilize sGC as well as to provide directed intracellular transfer of NO from NOS to sGC, thus preventing inactivation of NO by superoxide anion and formation of peroxynitrite, which is a toxic molecule that has been implicated in the pathology of several **vascular diseases**.

L60 ANSWER 14 OF 90 USPATFULL on STN

ACCESSION NUMBER: 2002:343870 USPATFULL

TITLE: Phosphoprotein target for insulin and its antagonists

INVENTOR(S): Cooper, Garth J.S., Auckland, NEW ZEALAND
Xu, Aimin, Auckland, NEW ZEALAND
Wang, Yu, Auckland, NEW ZEALAND

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002197596	A1	20021226
APPLICATION INFO.:	US 2002-114540	A1	20020401 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-280584P	20010330 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Randolph Ted Apple, Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA, 94304-1018
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1346
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides methods for diagnosing and treating individuals with insulin resistance.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L60 ANSWER 15 OF 90 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:832575 CAPLUS
DOCUMENT NUMBER: 137:346196
TITLE: Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent
INVENTOR(S): Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony; Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed
PATENT ASSIGNEE(S): Epigenesis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 872 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085308	A2	20021031	WO 2002-US13135	20020423
WO 2002085308	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XA13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XB13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XC13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-286137P P 20010424
WO 2002-US13135 A 20020423

OTHER SOURCE(S): MARPAT 137:346196

AB This patent relates to a compn. comprising a carrier, oligonucleotides (oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 receptor mRNA, one targeting adenosine A2b receptor, and two targeting an A3 receptor are capable of countering the effect of exogenously administered adenosine which is mediated by the specific receptor they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addn., they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. Treatment with antisense oligonucleotides in combination with anti-inflammatory steroid and/or ubiquinones is also provided. These agents and the compn. and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases assocd. with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and compn. may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

L60 ANSWER 16 OF 90 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-17971 BIOTECHDS
TITLE: A diagnostic assay for systemic vasculature events comprises assaying an array of markers and correlating the results; antibody immobilization and plasma protein fluorescent labelling for antibody microarray construction and diagnosis
AUTHOR: CHRISTOPHERSON R I; DOS REMEDIOS C G; CELERMAJER D S
PATENT ASSIGNEE: UNIV SYDNEY
PATENT INFO: WO 2002023191 21 Mar 2002
APPLICATION INFO: WO 2000-AU1141 12 Sep 2000
PRIORITY INFO: AU 2000-56 12 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-499804 [53]
AN 2002-17971 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Assessing (M1) the parameters associated with a condition of the systemic vasculature or assessing the risk of a condition of event occurring, is new.

DETAILED DESCRIPTION - Assessing the parameters associated with a condition of the systemic vasculature or assessing the risk of a condition of event occurring comprises analyzing a biological sample for a series of indicators and correlating the pattern of indicators with the condition and prognosis. INDEPENDENT CLAIMS are included for the following: (1) an array (I) of binding partners for members in a biological sample for use in (M1), where the members are present, absent, elevated or otherwise activated in a subject following a condition or event associated with the systemic vasculature where the binding partners are defined by (x,y) coordinates so that the array comprises n binding

partners at coordinates (x, y), (x2, y2)....(xn, yn) and where the pattern of interaction between the members and the binding partners is indicative of the condition or event; (2) estimating (M2) the size of an infarct (Is) or related condition based on the results of (M1), determined by the formula (F1); (3) assessing (M3) the parameters associated with a condition associated with the systemic vascularization comprising screening for the presence of two or more mRNA molecules by contacting the samples with an array of oligonucleotides capable of hybridizing or otherwise capturing the mRNA molecules; (4) a data processing means (II) for assessing a condition using (M1); (5) a treatment (M4) comprising assessing the condition by (M1) and effecting a suitable treatment regime, where the members tested are group (A): myoglobin, myosin light chain, myosin heavy chain, total creatine kinase, lactate dehydrogenase, aspartate aminotransferase, cardiac troponin I or T, fatty acid binding protein, glycogen phosphorylase-BB isoenzyme, alpha-atrial natriuretic peptide, cytoplasmic FABP, brain natriuretic peptide, adrenomedullin, low density lipoprotein, very low density lipoprotein, high density lipoprotein, intermediate density lipoprotein, C-reactive protein, serum amyloid A, P-selectin, prostaglandins, platelet-activating factor, histamine, TNF-alpha, sTNFR2, fibrin, fibrinogen, fibronolytic peptides, modified hemoglobin, ferritin, soluble intercellular adhesion molecule, **heat shock protein**, apoB, apoA, apoE, homocysteine, Streptococcus sp., Porphyromonas gingivalis, Helicobacter pylori, Chlamydia pneumoniae, necrosis and platelet markers, leptin, vasopeptidase inhibitor of cardiac endogenous kinins, heparin, metalloproetinase-9, metalloproteinase-1, angiotensin-converting enzyme, CD95/Apo1/Fas, hepatocyte growth factor, soluble vascular cell adhesion molecule-1, plasma brain natriuretic peptide, angiotensin II type receptor, endothelial constitutive nitric oxide synthase, glycoprotein IIIa genetic polymorphisms, factor VIIa, thrombin, endothelin-1, cardiac myofibrillar proteins or Fas, or ligands or binding partners of these members, or nucleic acids encoding them or their fragments, ligands or binding partners; (6) a computer program (II) for assessing the likelihood or risk of development of a condition or event associated with the systemic vasculature, comprising: (a) a code that recieves an input value for the presence or absence of one or more features selected from group (A); and (b) a computer readable medium that stores the code; and (7) a computer system (III) for assessing the likelihood of a subject with an event or condition associated with the systemic vascularization, comprising: (a) a machine readable storage medium comprising a data storage material encoded with machine readable data which comprises values for the presence or absence of one or more features selected from group (A);(b) a working memory for storing instructions for processing the machine readable data; (c) a central-processing unit coupled to the machine-readable data to provide a sum of the values corresponding to a predictive value for the candidate sequences; and (d) an output hardware coupled to the central processing unit for receiving the predictive values. Is=the integral between 0 and t of (f(t)dt x Bw x Kw)/ (Ed x Kr) (F1)Where: Is = infarct size; F(t) = member appearance function; F(t)dt = rate of release of a member in a biological sample, the member being present, absent, elevated or otherwise activated in a subject following a cardiovascular condition or event leading to the infarct; Bw = body weight of subject; Kw = proportion of body weight into which the member is released; Ed = rate of removal of the member from the evaluation; and Kr = total amount of member released divided by the amount of the member released from the infarcted tissue.

ACTIVITY - Cardiant; vascular; cerebroprotective; thrombolytic. No suitable data given.

MECHANISM OF ACTION - None given.

USE - (M1) is useful for assessing the parameters associated with a **vascular disease** (including cardiovascular, stroke, pulmonary, renovascular, cerebrovascular, thrombotic or generalized arterial or venous conditions or events), and (M4) is used to treat these diseases.

ADMINISTRATION - No details given.

ADVANTAGE - Early markers for cardiac events include myoglobin, creatine kinase MB isoform, cardiac troponin-T and cardiac troponin-I. Correlating the levels largely overcomes the problem of false positives. Medium and long term markers include total creatine kinase, cardiac troponin-I, aspartate aminotransferase, lactate dehydrogenase, myosin light chain, myosin heavy chain, fatty acid binding protein and ABC. The early and late markers can be used to estimate the size of the infarct.

EXAMPLE - No suitable example given.(89 pages)

L60 ANSWER 17 OF 90 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-12940 BIOTECHDS
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide;
vector expression in Escherichia coli for recombinant protein production and disease therapy
AUTHOR: PATTERSON W C; BALLINGER C A
PATENT ASSIGNEE: UNIV TEXAS SYSTEM
PATENT INFO: US 2002177212 28 Nov 2002
APPLICATION INFO: US 2001-13939 7 Dec 2001
PRIORITY INFO: US 2001-13939 7 Dec 2001; US 1999-134433 17 May 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-298777 [29]
AN 2003-12940 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A polypeptide (I) which negatively regulates binding of **heat shock protein** (Hsp) to a substrate or induces ubiquitylation of a heat shock bound substrate, has a sequence of 303, 304 or 289 amino acids, and is encoded by a nucleic acid that hybridizes to a sequence of 1286, 1218 or 1225 nucleotides, or a human carboxy terminus of a Hsc70 interacting protein genomic nucleotide sequence, is new.

DETAILED DESCRIPTION - An isolated polypeptide (I) which negatively regulates binding of a **heat shock protein** (Hsp) to a substrate or induces ubiquitylation of a heat shock bound substrate, comprises: (i) an amino acid sequence (S1) of 303, 304 or 289 amino acids, given in the specification; (ii) a sequence (S2) having greater than about 40 % sequence identity to (S1); or (iii) a polypeptide comprising amino acids 1 - 197 of (S2), encoded by a nucleic acid that hybridizes to a nucleic acid or a nucleic acid complement of a sequence (S3) comprising 1286, 1218, or 1225 nucleotides, or a human carboxy terminus of Hsc70 interacting protein (CHIP) genomic nucleotide sequence, given in the specification, under hybridization conditions (HC) of 0.015 M NaCl/0.0015 M sodium citrate (SSC) and about 0.1 % sodium dodecyl sulfate (SDS) at about 50 - 65 degreesC. INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid fragment (II) capable of hybridizing to (S3) or its complement under HC; (2) a nucleic acid vector containing (II); (3) a host cell comprising (II); (4) an isolated nucleic acid fragment comprising (S3) or its complement, or a nucleic acid sequence (S4) with 60 % nucleic acid identity to (S3) or its complement; (5) expressing (M) a nucleic acid fragment that encodes a polypeptide, the presence of which is associated with a negative regulation of a **heat shock protein** or ubiquitylation of a heat shock bound substrate, comprising expressing the nucleic acid fragment in a cultured host cell transformed with an expression vector comprising the nucleic acid fragment operably linked to control sequences recognized by the host cell; (6) producing a recombinant polypeptide; (7) inhibiting a nucleic acid that encodes a polypeptide that negatively regulates binding of a **heat shock protein** to a substrate or induces ubiquitylation of a heat shock bound substrate in a mammal, comprising administering to a mammal a composition comprising an amount of an inhibitor to an isolated nucleic acid fragment

having (S4) or its complement; and (8) an inhibitory composition (C) comprising an amount of an inhibitor to the isolated polypeptide which negatively regulates binding of Hsp to a substrate effective to immunize or treat a mammal for a neoplastic disease, ischemic disease or a disease characterized by inflammation.

BIOTECHNOLOGY - Preparation: (I) Is produced by: (a) providing an expression vector that comprises a nucleic acid fragment having (S4) or its complement, operably linked to control sequences recognized by a host cell; (b) transforming the host cell with the expression vector; and (c) culturing the transformed cell under conditions that allow expression of the recombinant polypeptide encoded by the nucleic acid fragment. Preferred Polypeptide: (I) Interacts with a S5a proteasome subunit of an ubiquitin-proteasome degradative pathway. A U-box domain of (I) interacts with a S5a proteasome subunit. (I) Is a recombinant polypeptide. (I) Has a molecular weight as determined by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis (PAGE) of about 30 - 40 kD. Preferred Nucleic Acid: The nucleic acid fragment encodes a portion of (I). Preferred Vector: The vector is an expression vector capable of producing a portion of (I). Preferred Cell: The host cell is prokaryotic or eukaryotic cell. Preferred Method: The prokaryotic host cell is a gram negative or gram positive organism. The host cell is an Escherichia coli cell. (M) further involves recovering the polypeptide from the host cell. Preferred Composition: (I) is in combination with a carrier.

ACTIVITY - Immunosuppressive; Antiinflammatory; Cardiant; Cerebroprotective; Cytostatic; Vasodilator; Vasotropic. No biological data is given.

MECHANISM OF ACTION - Binding of **heat shock protein** to substrate negative regulator; Ubiquitylation of heat shock bound substrate inducer (claimed).

USE - (I) Is useful for negatively regulating binding of Hsp, such as, Hsc70, Hsp70 or Hsp90 to a substrate or for inducing ubiquitylation of a heat shock bound substrate. (I) Is useful for identifying an inhibitor of (I), by: (a) incubating (I) with a compound under conditions that promote the negative regulating activity of the polypeptide or ubiquitylation activity of the polypeptide when the compound is not present; and (b) determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. (C) Is useful for inhibiting (I) in a mammal. (C) Is therapeutically effective for a neoplastic disease, ischemic disease or disease characterized by inflammation (claimed). (C) Is useful for treating, inhibiting or preventing neoplastic diseases such as cancer or lymphoma, ischemic diseases such as stroke, **vascular disease**, or myocardial infarction, or a disease characterized by inflammation, which includes infections and autoimmune diseases.

ADMINISTRATION - Administration is through local, systemic, parenteral, subcutaneous, intramuscular, or oral routes. No dosage is given.

EXAMPLE - cDNA cloning of a human, mouse, and Drosophila carboxy terminus of Hsc70 (**heat shock protein**) interacting protein (CHIP) was carried out as follows. A nucleic acid fragment corresponding to nucleotides 721 - 1150 of the human cyclophilin 40 (CyP-40) cDNA was radiolabeled with (alpha-32P)dCTP, and used to screen a phage library of human heart DNA in the vector lambdagt11. Phage colonies were grown on agarose and transferred to nitrocellulose membranes. Phage colonies that hybridized preferentially under low-stringency conditions (0.2 x saline sodium citrate (SSC), 0.1 % sodium dodecyl sulfate (SDS) at 42 degrees Centigrade) were analyzed and characterized. A total of 12 colonies were characterized by plaque isolation, amplification and sequencing, and it was determined that eight colonies contained human CyP-40 cDNA sequences, and four colonies encoded a new cDNA having no sequence identity to known genes available in GenBank (RTM). The new cDNA was analyzed using Basic Local Alignment Search Tool (BLAST) and GenBank (RTM) databases. Human expressed sequence

tag (EST) sequences found to be identical to the cDNA sequence of the new cDNA obtained by phage screening were Clone ID Nos: 548268, 177869, and 647520. Clones 548268 and 177869 contained polyadenylated sequence at the 3' end. The 5' end of the cDNA was defined by 5' rapid amplification of cDNA ends using human heart mRNA and primers designed on the basis of EST sequences P1 and P2. Products of these reactions, as well as plasmids containing the EST fragments, were sequenced and a single contiguous human cDNA sequence was assembled. Homologous mouse and Drosophila cDNAs (comprising a sequence of 1218 and 1225 nucleotides fully defined in the specification, respectively) were identified in a similar manner, based on EST clones ID Nos. 525111 and 546365 (mouse) and clone ID No. LD16049 (Drosophila). Sequence comparisons were made using GeneWorks 2.5.1 (RTM) software using the CLUSTRAL (RTM) alignment default parameters. gctgtaagctcgctgcagat (P1) gcctcatcatagctctccatctc (P2)(50 pages)

L60 ANSWER 18 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4

ACCESSION NUMBER: 2002:383033 BIOSIS
DOCUMENT NUMBER: PREV200200383033
TITLE: Down-regulation of monocyte apoptosis by phagocytosis of platelets: Involvement of a caspase-9, caspase-3, and heat shock protein 70-dependent pathway.
AUTHOR(S): Lang, Detlef (1); Dohle, Frank; Terstesse, Martin; Bangen, Philip; August, Christian; Pauels, Hans-Gerd; Heidenreich, Stefan
CORPORATE SOURCE: (1) Department of Medicine D, University Hospital Muenster, Albert-Schweitzer-Strasse 33, D-48129, Muenster: langd@uni-muenster.de Germany
SOURCE: Journal of Immunology, (June 15, 2002) Vol. 168, No. 12, pp. 6152-6158. http://www.jimmunol.org/. print. ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Monocytes interact and cross-talk with platelets in many settings including inflammation, hemostasis, or **vascular disorders**. During inflammatory diseases, there is a rapid targeting of monocytes and platelets to points of inflammation and endothelial injury, where they lie side-by-side. In this in vitro study, we investigated different interactions between monocytes and platelets and elucidated whether platelets might affect monocyte apoptosis. Freshly isolated human monocytes were rendered apoptotic by serum deprivation or CD95 ligation and cocultured with platelets. Monocyte apoptosis was determined by flow cytometry, TUNEL staining, DNA electrophoresis, and transmission electron microscopy imaging. We could show that monocyte apoptosis was highly suppressed when platelets were added to the cultures. Transmission electron microscopy depicted that monocytes completely ingested thrombocytes by phagocytosis. Blocking thrombocyte uptake by the phagocytosis inhibitor cytochalasin D abrogated the enhanced monocyte survival and led to high apoptosis levels. Monocyte survival was paralleled by down-regulation of caspase-9 and -3 and up-regulation of **heat shock protein** 70 during uptake of platelets. Platelet supernatants and contents of platelet granules were ineffective in altering monocyte senescence. Also, ingestion of latex beads or zymosan by monocytes was ineffective to mimic platelet-dependent rescue from apoptosis. In conclusion, this study shows that platelets can suppress apoptosis of monocytes by a specific phagocytosis-dependent process with further consequences for atherosclerotic or inflammatory conditions.

L60 ANSWER 19 OF 90 TOXCENTER COPYRIGHT 2003 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2002:196706 TOXCENTER
COPYRIGHT: Copyright 2003 ACS
DOCUMENT NUMBER: CA13712166924B
TITLE: Heat shock proteins, inflammation, and cardiovascular disease

AUTHOR(S): Pockley, A. Graham
CORPORATE SOURCE: Division of Clinical Sciences (North), Northern General Hospital, University of Sheffield, Sheffield, UK.
SOURCE: Circulation, (2002) Vol. 105, No. 8, pp. 1012-1017. CODEN: CIRCAZ. ISSN: 0009-7322.
COUNTRY: UNITED KINGDOM
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:231551
LANGUAGE: English
ENTRY DATE: Entered STN: 20020910
Last Updated on STN: 20030624

AB A review on the immune basis of **vascular disease**, **heat-shock proteins** (Hsps) and their induction, Hsp and the immune response, Hsp expression and Hsp reactivity in **vascular disease**, Hsps as inducers and mediators of **vascular disease**, Hsps as autoantigens, and the role of infection in pathogenesis of atherosclerosis.

L60 ANSWER 20 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002280086 EMBASE
TITLE: [The role inflammation and infection in pathogenesis atherosclerosis].
ULOHA INFEKCIE A ZAPALU V PATOGENEZE ATEROSKLEROZY.
AUTHOR: Jaber J.; Murin J.; Kinova S.; Gavornik P.; Ghanem Wisam M.A.; Radman A.; Gharaibeh A.; Richter P.
CORPORATE SOURCE: Dr. J. Jaber, I Interna Klinika, Fakultna Nemoenica, Mickiewiczova 13, 813 69 Bratislava, Slovakia
SOURCE: Vnitrni Lekarstvi, (2002) 48/7 (657-666). Refs: 60
ISSN: 0042-773X CODEN: VNLEAH
COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: Slovak
SUMMARY LANGUAGE: English; Slovak

AB Pathogenesis of the atherosclerotic process is deemed as multifactorial. To the most important risk factors, besides certain family predisposition, there belongs hypercholesterolemia, arterial hypertension, obesity, diabetes mellitus, smoking and others. In the last years there are more and more data about the role of inflammation and infection in the whole development of atherosclerosis. The witness for this hypothesis is the findings of high parameters of inflammation in involved vessels as well as in the blood of atherosclerosis suffering persons. Opinions about the inflammation theory appear from the 90th. Local sterile inflammation in the subendotelium of the middle and big arteries has been proved to consist of specific immune reaction (activation of the T-lymphocytes) as well as nonspecific characteristic by elevated monocytes in the artery wall during the whole process of atherogenesis. Inflammation in the plaque can trigger and hold several factors engaged in the atherosclerotic process, such as oxidized LDL cholesterol, elevated production of various superoxides, activated macrophages, activated T-lymphocytes, cytokines (IL-1, IL-6, interferon gama) and lipoprotein Lp (a). In this inflammation process levels of CRP (acute phase protein), fibrinogen and erythrocyte sedimentation are elevated as a reaction of the organism to nonspecific chronic infections. Because of this it is thought that elevated fibrinogen and erythrocyte sedimentation are markers of the cardiovascular risk. Some papers deal with antiinflammatory effects of statins, because these lower CRP levels so they also lower atherosclerotic risk through not only lowering of cholesterol levels. Also aspirine, as an antiinflammation agent, changing the CRP levels, would be of benefit for pacients with **vascular disease** because its antiaggregation and antiinflamatory effects. ACE inhibitors are also antiinflamatory through blocking of tissue production of angiotensin II (artery wall and

atherosclerotic plaque). Enzymatic inhibitors changing angiotensis can also have a partial antiinflammatory effect. The infection theory is supported also by tracing of some microorganisms in the atherosclerotic plaque or in the blood, as e. g. Helicobacter pylori or Chlamydia pneumoniae; to the autoimmune origin is indicated the presence of the specific immunity reaction against **heat shock proteins** (HSP) or oxidized LDL. This infection theory offers new therapy possibilities. Therefore eradication for example by antibiotics can lead to stabilization of the atherosclerotic plaque with positive consequences, as it was discovered by many studies.

L60 ANSWER 21 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 6
ACCESSION NUMBER: 2002197680 EMBASE
TITLE: Regulation of endothelial Nitric Oxide Synthase activity and gene expression.
AUTHOR: Wu K.K.
CORPORATE SOURCE: K.K. Wu, Vascular Biology Research Center, Division of Hematology, Univ. of Texas-Houston Med. School, Houston, TX, United States. kenneth.k.w@uth.tmc.edu
SOURCE: Annals of the New York Academy of Sciences, (2002) 962/- (122-130).
Refs: 58
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Endothelial nitric oxide synthase (eNOS) is constitutively expressed in endothelial cells lining the blood vessel and the heart. It plays a major role in vascular and tissue protection. Its activity is tightly controlled by an intramolecular autoinhibitory element that hinders calmodulin binding. This molecular hindrance is removed by elevated intracellular calcium levels. The catalytic activity of eNOS is augmented by phosphorylation of a C-terminal serine residue (Ser-1177 of human eNOS) through the phosphatidyl-3 kinase (PI-3K)/Akt pathway. Its activity is also enhanced by binding to **heat shock protein** -90. These two processes are calcium independent. The two biochemical events appear to facilitate calmodulin access to its binding site. eNOS is upregulated at the transcriptional level. Its upregulation is mediated by an increased Sp1 binding to its cognate site on eNOS promoter/enhancer region via the action of protein phosphatase 2A (PP2A). PP2A is activated by a signaling pathway including PI-3.gamma. .fwdarw. Janus activated kinase 2 (Jak2) .fwdarw. MEK-1 .fwdarw. ERK1 and 2. The transcriptional and posttranslational enhancement of eNOS activity is two- to threefold above the basal level. A higher magnitude of augmentation of eNOS gene expression can be achieved by gene transfer, which confers protection against **vascular diseases** and ischemia-induced tissue injury in experimental animals. These findings provide new insight into the protective role of eNOS and the therapeutic potential of eNOS gene therapy.

L60 ANSWER 22 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7
ACCESSION NUMBER: 2002:563091 BIOSIS
DOCUMENT NUMBER: PREV200200563091
TITLE: Chlamydia pneumoniae activates IKK/IkappaB-mediated signaling, which is inhibited by 4-HNE and following primary exposure.
AUTHOR(S): Donath, Bernadette; Fischer, Claudia; Page, Sharon; Prebeck, Sigrid; Jilg, Nikolaus; Weber, Marion; da Costa, Clarissa; Neumeier, Dieter; Miethke, Thomas; Brand, Korbinian (1)
CORPORATE SOURCE: (1) Institute of Clinical Chemistry and Pathobiochemistry,

Klinikum rechts der Isar, Technische Universitaet Muenchen, Ismaninger Strasse 22, 81675, Muenchen: brand@klinchem.med.tu-muenchen.de Germany

SOURCE: Atherosclerosis, (November, 2002) Vol. 165, No. 1, pp. 79-88. http://www.elsevier.com/locate/atherosclerosis. print.
ISSN: 0021-9150.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Chlamydia pneumoniae may be involved in atherosclerosis by inducing inflammation as well as LDL oxidation. The transcription factor NF-kappaB is found in an active state in atherosclerotic lesions. This study examined the effect of C. pneumoniae exposure on the NF-kappaB system in human monocytic lineage cells. Short exposure to C. pneumoniae as well as chlamydial **heat shock protein** 60 activated NF-kappaB, accompanied by increased cytokine production. Incubation with C. pneumoniae induced depletion of IkappaB-alpha and later IkappaB-epsilon which was preceded by IkappaB kinase complex activation. 4-Hydroxynonenal, an aldehyde LDL oxidation product, was shown to inhibit C. pneumoniae induced NF-kappaB activation by preventing IkappaB phosphorylation/proteolysis. During long-term incubation with C. pneumoniae IkappaB-alpha returned to baseline, whereas the levels of IkappaB-epsilon and p65 were upregulated. Interestingly, long-term preincubation with C. pneumoniae selectively prevented restimulation by this microorganism, which appears to be at least partly facilitated by inhibition of IkappaB proteolysis. C. pneumoniae-induced NF-kappaB activation as well as the inhibition of that effect under certain conditions may contribute to chronic inflammation with potential relevance to **vascular disease**.

L60 ANSWER 23 OF 90 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:52338 CAPLUS

DOCUMENT NUMBER: 138:285274

TITLE: Genomic analysis of immediate/early response to shear stress in human coronary artery endothelial cells

AUTHOR(S): Peters, D. G.; Zhang, X.-C.; Benos, P. V.; Heidrich-O'Hare, E.; Ferrell, R. E.

CORPORATE SOURCE: Departments of Human Genetics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: Physiological Genomics (2002), 12(1), 25-33
CODEN: PHGEFP; ISSN: 1094-8341
URL: http://physiolgenomics.physiology.org/cgi/reprint/12/1/25.pdf

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB The involvement of shear stress in the pathogenesis of vascular disease has motivated efforts to define the endothelial cell response to applied shear stress in vitro. A central question has been the mechanisms by which endothelial cells perceive and respond to changes in fluid flow. The authors have utilized cDNA microarrays to characterize the immediate/early genomic response to applied laminar shear stress (LSS) in primary cultures of human coronary artery endothelial cells (HCAECs). Cells were exposed, in a parallel plate flow chamber, to 0, 15, or 45 dyn/cm2 LSS for 1 h, and gene expression profiles were detd. using human GEM1 cDNA microarrays. The authors find that a high proportion of LSS-responsive genes are transcription factors, and these are related by their involvement in growth arrest. These likely play a central role in the reprogramming of endothelial homeostasis following the switch from a static to a shear-stressed environment. LSS-responsive genes were also found to encode factors involved in vasoreactivity, signal transduction, antioxidants, cell cycle-assocd. genes, and markers of cytoskeletal function and dynamics.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 24 OF 90 TOXCENTER COPYRIGHT 2003 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2002:66915 TOXCENTER
COPYRIGHT: Copyright 2003 ACS
DOCUMENT NUMBER: CA13518251960P
TITLE: Suppression of **vascular disorders** by mucosal administration of **heat shock protein** peptides
AUTHOR(S): Weiner, Howard L.; Maron, Ruth; Libby, Peter
CORPORATE SOURCE: ASSIGNEE: Brigham and Women's Hospital, Inc.
PATENT INFORMATION: WO 2001068124 A2 20 Sep 2001
SOURCE: (2001) PCT Int. Appl., 49 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2001:693117
LANGUAGE: English
ENTRY DATE: Entered STN: 20020319
Last Updated on STN: 20020319

AB Methods are disclosed for treating vascular disorders in mammals. The methods involve administering one or more agents selected from a heat shock protein, a therapeutically effective fragment and a therapeutically effective analog of a heat shock protein in a form suitable for mucosal administration. In some embodiments the heat shock protein of the method is mycobacterial HSP65. In some embodiments the heat shock protein is human HSP60. In some embodiments the heat shock protein is chlamydial HSP60. The method is of particular value in the treatment of atherosclerosis. Also disclosed are compns. useful for treating vascular disorders in mammals. The compns. include one or more agents selected from heat shock protein, therapeutically effective fragments and therapeutically effective analogs of the heat shock protein in aerosol or oral form. In some embodiments the heat shock protein of the compn. is mycobacterial HSP65. In some embodiments the heat shock protein of the method is human HSP60. In some embodiments the heat shock protein is chlamydial HSP60. The compns. is of particular value in the treatment of atherosclerosis.

L60 ANSWER 25 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 9
ACCESSION NUMBER: 2001:345428 BIOSIS
DOCUMENT NUMBER: PREV200100345428
TITLE: Heat shock proteins, anti-heat shock protein reactivity and allograft rejection.
AUTHOR(S): Pockley, A. Graham (1)
CORPORATE SOURCE: (1) Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield, S5 7AU UK
SOURCE: Transplantation (Baltimore), (June 15, 2001) Vol. 71, No. 11, pp. 1503-1507. print.
ISSN: 0041-1337.
DOCUMENT TYPE: Article; General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Heat shock proteins** are families of highly conserved immunodominant molecules, reactivity to which has been implicated in the pathogenesis of a number of autoimmune and **vascular disease** states. However, **heat shock proteins** are cytoprotective, and in clinical and experimental arthritis, anti-**heat shock protein** reactivity can down modulate immune responses via a self-Hsp reactive, Th2-type mechanism. Despite a number of studies associating **heat shock protein** expression and anti-**heat shock protein** reactivity with

allograft rejection, the balance between protective and damaging effects and the precise influence of these responses on graft outcome is unclear. This article reviews current knowledge surrounding **heat shock proteins**, autoinununity, and allograft rejection and presents a perspective on the potential influence of these proteins and the stress response on allograft outcome.

L60 ANSWER 26 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 10
ACCESSION NUMBER: 2001:281022 BIOSIS
DOCUMENT NUMBER: PREV200100281022
TITLE: Comparative study on antibodies to human and bacterial 60 kDa heat shock proteins in a large cohort of patients with coronary heart disease and healthy subjects.
AUTHOR(S): Prohaszka, Z. (1); Duba, J.; Horvath, L.; Csaszar, A.; Karadi, I.; Szebeni, A.; Singh, M.; Fekete, B.; Romics, L.; Fust, G.
CORPORATE SOURCE: (1) 3rd Department of Medicine, Semmelweis University, Budapest, Kutvolgyi ut 4, H-1125, Budapest: prohoz@kut.sote.hu Hungary
SOURCE: European Journal of Clinical Investigation, (April, 2001) Vol. 31, No. 4, pp. 285-292. print.
ISSN: 0014-2972.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Recent observations indicate an association between antibodies against mycobacterial **heat shock protein** (**hsp65**) and coronary heart disease (CHD). Previously, we reported on marked differences in antigen specificity and complement activating ability of anti-**hsp65** antibodies and auto-antibodies against human **heat shock protein**, **hsp60**.
Here, we investigated whether there are differences between antih-sp65 and anti-**hsp60** antibodies in their association with CHD. Design: We measured by ELISA the levels of antibodies to **hsp65**, **hsp60** and E. coli-derived GroEL in three groups: Group I, 357 patients with severe CHD who underwent by-pass surgery; Group II, 67 patients with negative coronary angiography; Group III, 321 healthy blood donors. Antibodies against Helicobacter pylori were also measured by commercial ELISA. Results: As calculated by multiple regression analysis, the levels of anti-**hsp60** auto-antibodies were significantly higher in Group I compared to Group II ($P = 0.007$) or Group III ($P < 0.0001$). By contrast, although concentrations of anti-**hsp65** and anti-GroEL antibodies in Group I were higher than in Group III, no significant differences between Group I and Group II were found. Antibodies to the two bacterial hsp strongly correlated to each other, but either did not correlate or weakly correlated to **hsp60**. In Group I, serum concentrations of anti-H.pylori antibodies significantly correlated with those of anti-**hsp65** and anti-GroEL antibodies but they did not correlate with the anti-**hsp60** antibodies.
Conclusion: As to their clinical relevance, a remarkable difference become evident between antibodies to human **hsp60** and antibodies against bacterial hsp in the extent of association with CHD. On the basis of these findings and some pertinent literature data, an alternative explanation for the association between high level of anti-hsp antibodies and atherosclerotic **vascular diseases** is raised.

L60 ANSWER 27 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 11
ACCESSION NUMBER: 2001373541 EMBASE
TITLE: Influence of caveolin, cholesterol, and lipoproteins on nitric oxide synthase: Implications for vascular disease.
AUTHOR: Everson W.V.; Smart E.J.
CORPORATE SOURCE: E.J. Smart, Department of Physiology, University of Kentucky, Chandler Medical Center, 800 Rose Street,

Lexington, KY 40536, United States. ejsmart@pop.uky.edu
SOURCE: Trends in Cardiovascular Medicine, (2001) 11/6 (246-250).
Refs: 43
ISSN: 1050-1738 CODEN: TCMDEQ
PUBLISHER IDENT.: S 1050-1738(01)00119-0
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Caveolin-1 traffics cholesterol between the endoplasmic reticulum and cell surface caveolae in a non-vesicle chaperone complex which contains **heat shock protein** 56, cyclophilin 40, and cyclophilin A. Recent studies demonstrate that endothelial nitric oxide synthase (eNOS), caveolin, hetero-trimeric G-protein coupled receptors, and a calcium channel form an activation complex that is associated with cholesterol-rich caveolae. Oxidized LDL depletes caveolae of cholesterol and prevents agonist stimulation of eNOS by disrupting the activation complex. HDL antagonizes the effects of oxLDL by donating cholesterol to caveolae, thereby preserving the structure and function of caveolae. These findings and others provide a possible mechanistic basis for some of the molecular changes observed in **vascular disease**.
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L60 ANSWER 28 OF 90 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED.
on STN DUPLICATE 12
ACCESSION NUMBER: 2001-0400820 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Multilateral in vivo and in vitro protective effects of the novel heat shock protein coinducer, bimoclomol : Results of preclinical studies
AUTHOR: NANASI P. P.; JEDNAKOVITS A.
CORPORATE SOURCE: Department of Physiology, University Medical School of Debrecen, Hungary; Biorex Research and Development Co., Veszprem, Hungary
SOURCE: Cardiovascular drug reviews, (2001), 19(2), 133-151, 49 refs.
ISSN: 0897-5957
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-21845, 354000097095520040
AN 2001-0400820 PASCAL
CP Copyright .COPYRGT. 2001 INIST-CNRS. All rights reserved.
AB Bimoclomol, the recently developed non-toxic **heat shock protein** (HSP) coinducer, was shown to display multilateral protective activities against various forms of stress or injuries at the level of the cell, tissue or organism. The compound enhanced the transcription, translation and expression of the 70 kD **heat shock protein** (HSP-70) in myogenic and HeLa cell lines exposed to heat stress, and increased cell survival on exposure to otherwise lethal thermal injury. Bimoclomol increased contractility of the working mammalian heart, this effect was associated with the increased intracellular calcium transients due to increased probability of opening of ryanodine receptors in the sarcoplasmic reticulum (SR). In healthy tissues these cardiac effects were evident only at relatively high concentrations of the drug, while in the ischemic myocardium bimoclomol exerted significant cardioprotective and antiarrhythmic effects at submicromolar concentrations. It decreased ischemia-induced reduction of contractility and of cardiac output, and dramatically

decreased the elevation of the ST-segment during ischemia as well as the occurrence of ventricular fibrillation upon reperfusion. Bimoclomol was also active in various pathological animal models subjected to acute or chronic stress. In the spontaneously hypertensive rats chronic pretreatment with bimoclomol restored sensitivity of aortic rings to acetylcholine; this effect was accompanied by accumulation of HSP-70 in the tissues. Bimoclomol pretreatment significantly diminished the consequences of **vascular disorders** associated with diabetes mellitus. Diabetic neuropathy, retinopathy, and nephropathy were prevented or diminished, while wound healing was enhanced by bimoclomol. Enhancement of wound healing by bimoclomol was observed after thermal injury as well as following ultraviolet (UV) irradiation. In addition to the beneficial effects on peripheral angiopathies, bimoclomol antagonized the increase in permeability of blood-brain barrier induced by subarachnoid hemorrhage or arachidonic acid. A general and very important feature of the above effects of bimoclomol was that the drug failed to cause alterations under physiological conditions (except the enhanced calcium release from cardiac sarcoplasmic reticulum). Bimoclomol was effective only under conditions of stress. Consistent with its HSP-coinducer property, bimoclomol alone had very little effect on HSP production. Its protective activity became apparent only in the presence of cell damage. Currently, bimoclomol reached the end of the Phase II clinical trial in a group of 410 patients with diabetic complications. Results of this trial will answer the question, whether a compound with promising in vitro and in vivo pre-clinical findings will produce the anticipated beneficial effects in humans. In the event of a positive outcome of this trial, the indications for bimoclomol will be substantially extended.

L60 ANSWER 29 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001138211 EMBASE
TITLE: Role of **heat shock protein** 70 in **vascular disease**.
AUTHOR: Stansby G.; Chan Y.-C.
CORPORATE SOURCE: Prof. G. Stansby, Northern Vascular Centre, Freeman Hospital, Newcastle-upon-Tyne NE7 7DN, United Kingdom. gerard.stansby@nuth.northy.nhs.uk
SOURCE: Critical Ischaemia, (2001) 11/1 (15-21).
Refs: 53
ISSN: 0956-2257 CODEN: CRISE3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English

L60 ANSWER 30 OF 90 TOXCENTER COPYRIGHT 2003 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 2000:218218 TOXCENTER
COPYRIGHT: Copyright 2003 ACS
DOCUMENT NUMBER: CA13401002328X
TITLE: Human heat shock protein 60 in diagnosis and treatment of atherosclerosis and coronary heart disease
AUTHOR(S): Singh, Mahavir; Prohaszka, Zoltan; Fust, Gyorgy; Romics, Laszlo
CORPORATE SOURCE: ASSIGNEE: Semmelweis University of Medicine
PATENT INFORMATION: WO 2000072023 A2 30 Nov 2000
SOURCE: (2000) PCT Int. Appl., 47 pp.
CODEN: PIXXD2.
COUNTRY: HUNGARY
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:842379
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020305

AB The present invention concerns novel uses for human **HSP60** (**heat shock protein** 60) in methods of treatment or diagnosis of the human body, more particularly diagnostic test methods, the manuf. of diagnostic tests, and diagnostic test kits for patients with **vascular disorders** due to atherosclerosis, having a tendency to **heat shock protein**-induced complement activation, for example to myocardial disorders such as coronary heart disease. Blood samples were applied to microtiter plates coated with recombinant hHSP60 and anti-hHSP60 antibodies were allowed to bind. Unbound material was washed away and peroxidase conjugated anti-complement C4b was added to detect complement activation. There was a pos. correlation between the level of anti-hHSP60 antibodies and coronary heart disease due to atherosclerosis. Children at risk due to family history had significantly elevated levels as well.

L60 ANSWER 31 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14
ACCESSION NUMBER: 2001:71555 BIOSIS
DOCUMENT NUMBER: PREV200100071555
TITLE: Estrogen signals to the preservation of endothelial cell form and function.
AUTHOR(S): Razandi, Mahnaz; Pedram, Ali; Levin, Ellis R. (1)
CORPORATE SOURCE: (1) Medical Service, Long Beach Veterans Affairs Medical Ctr., 5901 E. 7th St., (111-I), Long Beach, CA, 90822: ellis.levin@med.va.gov USA
SOURCE: Journal of Biological Chemistry, (December 8, 2000) Vol. 275, No. 49, pp. 38540-38546. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Estrogen is important for the primary prevention of **vascular disease** in young women, but the mechanisms of protection at the vascular cell are still largely unknown. Although traditionally thought of as a nuclear transcription factor, the estrogen receptor has also been identified in the cell plasma membrane to signal but serve largely undefined roles. Here we show that estradiol (E2) rapidly activates p38beta mitogen-activated protein kinase in endothelial cells (EC), which activates the mitogen-activated protein kinase-activated protein kinase-2 and the phosphorylation of **heat shock protein** 27. The sex steroid preserves the EC stress fiber formation and actin and membrane integrity in the setting of metabolic insult. E2 also prevents hypoxia-induced apoptosis and induces both the migration of EC and the formation of primitive capillary tubes. These effects are reversed by the inhibition of p38beta, by the expression of a dominant-negative mitogen-activated protein kinase-activated protein kinase-2 protein, or by the expression of a phosphorylation site mutant **heat shock protein** 27. E2 signaling from the membrane helps preserve the EC structure and function, defining potentially important vascular-protective effects of this sex steroid.

L60 ANSWER 32 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 15
ACCESSION NUMBER: 2000:410512 BIOSIS
DOCUMENT NUMBER: PREV200000410512
TITLE: Infections, immunity, and atherosclerosis: Associations of antibodies to Chlamydia pneumoniae, Helicobacter pylori, and cytomegalovirus with immune reactions to heat-shock protein 60 and carotid or femoral atherosclerosis.
AUTHOR(S): Mayr, Manuel; Kiechl, Stefan; Willeit, Johann; Wick, Georg; Xu, Qingbo (1)
CORPORATE SOURCE: (1) Institute for Biomedical Aging Research, Austrian Academy of Sciences, Rennweg 10, A-6020, Innsbruck Austria
SOURCE: Circulation, (August 22, 2000) Vol. 102, No. 8, pp. 833-839. print.

ISSN: 0009-7322.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Atherogenesis involves inflammatory processes in which infections are incriminated as possible contributors. Methods and Results: We evaluated cardiovascular risk factors as well as seropositivity to Chlamydia pneumoniae, Helicobacter pylori, and cytomegalovirus in a population-based study. A significant association between prevalence and severity of atherosclerosis in carotid and femoral arteries and IgA antibodies to C pneumoniae was demonstrated that was not substantially altered after adjustment for established risk factors. For anti-H pylori IgG antibodies, significant correlations to **vascular disease** were restricted to low social status and lesions in carotid arteries. In addition, the study design allowed us to monitor lesion progression over time. In this prospective analysis, C pneumoniae seropositivity emerged as a significant risk predictor. Antibody titers against cytomegalovirus were not a marker for prevalence or incidence of atherosclerosis in this population. Further infection parameters added to the predictive value of chlamydial serology in risk assessment: Mean odds ratios for the prevalence of carotid atherosclerosis were 4.2 and 6.3 for seropositive subjects with elevated C-reactive protein levels and clinical evidence for chronic respiratory infection, respectively. For subjects with all 3 infection parameters, the odds ratio of carotid atherosclerosis reached 10.3 (P<0.0001). Concomitantly, serum antibodies to mycobacterial **heat-shock protein** 65 (mHSP65) correlated with seropositivity to C pneumoniae and H pylori but not to cytomegalovirus. Conclusions: This prospective population-based study provides strong evidence for a potential atherogenic role of persistent bacterial infection, especially C pneumoniae, as indicated by serological and clinical data and demonstrates a correlation between immune reactions to mHSP65 and bacterial infections in atherogenesis.

L60 ANSWER 33 OF 90 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:52868 SCISEARCH
THE GENUINE ARTICLE: 388DV
TITLE: **Heat shock protein** expression by peripheral blood leukocytes in patients with **vascular disease**
AUTHOR: Wright B H (Reprint); Pockley A G
CORPORATE SOURCE: No Gen Hosp, Ctr Clin Sci, Sheffield S5 7AU, S Yorkshire, England
COUNTRY OF AUTHOR: England
SOURCE: CELL STRESS & CHAPERONES, (NOV 2000) Vol. 5, No. 5, pp. 498-498.
Publisher: CELL STRESS SOC INTERNATIONAL, UNIV CONNECTICUT, DEPT M C B, 75 NORTH EAGLEVILLE RD, U-44, STORRS, CT 06269-3044 USA.
ISSN: 1355-8145.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L60 ANSWER 34 OF 90 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:52866 SCISEARCH
THE GENUINE ARTICLE: 388DV
TITLE: Serum **Hsp60**, Hsp70, and anti-Hsp antibody levels in peripheral and renal **vascular disease**
AUTHOR: Wright B H (Reprint); Corton J M; El-Nahas A M; Wood R F M; Pockley A G
CORPORATE SOURCE: No Gen Hosp, Ctr Clin Sci, Sheffield S5 7AU, S Yorkshire, England
COUNTRY OF AUTHOR: England
SOURCE: CELL STRESS & CHAPERONES, (NOV 2000) Vol. 5, No. 5, pp. 497-497.

Publisher: CELL STRESS SOC INTERNATIONAL, UNIV CONNECTICUT, DEPT M C B, 75 NORTH EAGLEVILLE RD, U-44, STORRS, CT 06269-3044 USA.
ISSN: 1355-8145.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L60 ANSWER 35 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 16
ACCESSION NUMBER: 2000:442408 BIOSIS
DOCUMENT NUMBER: PREV200000442408
TITLE: Circulating heat shock protein 60 is associated with early cardiovascular disease.
AUTHOR(S): Pockley, A. Graham (1); Wu, Ruhia; Lemne, Carola; Kiessling, Rolf; de Faire, Ulf; Frostegard, Johan
CORPORATE SOURCE: (1) Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield, S5 7AU UK
SOURCE: Hypertension (Baltimore), (August, 2000) Vol. 36, No. 2, pp. 303-307. print.
ISSN: 0194-911X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The phylogenetically conserved nature of **heat shock proteins** (Hsp) has led to the proposition that they may provide a link between infection and the inflammatory component to **vascular disease**. Hypertension is associated with atherosclerosis. Here, we measured circulating **heat shock protein** and **heat shock protein** antibody levels in association with borderline hypertension. Seventy-two men with borderline hypertension patients and 75 normotensive control subjects (diastolic blood pressure 85 to 94 and <80 mm Hg, respectively) were selected from a population-screening program. The levels of **Hsp60**; Hsp70; and anti-human **Hsp60**, anti-human Hsp70, and anti-mycobacterial **Hsp65** antibodies were determined with enzyme immunoassay. The presence of carotid atherosclerosis and the intima-media thickness values were determined with ultrasonography. A major novel observation in this report was the detection of circulating **Hsp60**, which was present at a significantly enhanced level in patients with borderline hypertension. Furthermore, serum **Hsp60** was associated with intima-media thicknesses ($P<0.01$). Anti-**Hsp65** antibody levels were higher in borderline hypertension ($P<0.001$), whereas Hsp70 and anti-Hsp70 antibody levels did not differ. In contrast to anti-**Hsp65** antibody, anti-**Hsp60** antibody levels were lower in borderline hypertension ($P<0.03$), although the difference was quantitatively small. None of the parameters evaluated were associated with atherosclerosis, metabolic factors, or smoking. We identified elevated **Hsp60** levels in patients with borderline hypertension and an association between early atherosclerosis and **Hsp60** levels. The physiological role of **Hsp60** release has yet to be defined, but given the proinflammatory properties, these proteins could be involved in the induction/progression of both hypertension and atherosclerosis, as well as being markers for early cardiovascular disease.

L60 ANSWER 36 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:84713 BIOSIS
DOCUMENT NUMBER: PREV200100084713
TITLE: **Heat shock protein** expression by peripheral blood leukocytes in patients with **vascular disease**.
AUTHOR(S): Wright, Barbara H. (1); Pockley, A. Graham (1)
CORPORATE SOURCE: (1) Division of Clinical Sciences, Northern General

Hospital, Sheffield, S5 7AU UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 39. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L60 ANSWER 37 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 17
ACCESSION NUMBER: 2000:436729 BIOSIS
DOCUMENT NUMBER: PREV200000436729
TITLE: Elevated levels of circulating **heat shock protein** 70 (Hsp70) in peripheral and renal **vascular disease**.
AUTHOR(S): Wright, Barbara H.; Corton, Julia M.; El-Nahas, A. Meguid; Wood, Richard F. M.; Pockley, A. Graham (1)
CORPORATE SOURCE: (1) Section of Surgery, Division of Clinical Sciences (NGH), Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield, S5 7AU UK
SOURCE: Heart and Vessels, (2000) Vol. 15, No. 1, pp. 18-22. print.
ISSN: 0910-8327.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Heat shock proteins** (Hsp) are families of phylo-genetically conserved molecules that have a range of cytoprotective and intracellular functional roles. Reactivity to **heat shock proteins** has been implicated in the development of autoimmune disease and tissue expression of **heat shock proteins** and increased levels of anti-Hsp antibodies have also been reported in **vascular disease**. This study compared circulating levels of **Hsp60** and Hsp70 and antihuman **Hsp60**, antihuman Hsp70, and antimycobacterial **Hsp65** antibodies in peripheral (PVD) and renal (RVD) **vascular disease** with those in age- and sex-matched controls. Levels of Hsp70 were higher in both PVD (median 580 vs 40; $P < 0.01$) and RVD (median 160 vs 0; $P < 0.03$), whereas there were no differences in **Hsp60** levels. Anti-**Hsp60** antibody levels were elevated in PVD (146 vs 81 arbitrary units/ml; $P < 0.04$), but not RVD. This is the first study to demonstrate increased levels of circulating Hsp70 in pathological disease states; however, its physiological role remains to be determined.

L60 ANSWER 38 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 18
ACCESSION NUMBER: 2000017207 EMBASE
TITLE: Small molecular weight heat shock-related protein, Hsp20, exhibits an anti-platelet activity by inhibiting receptor-mediated calcium influx.
AUTHOR: Niwa M.; Kozawa O.; Matsuno H.; Kato K.; Uematsu T.
CORPORATE SOURCE: Dr. M. Niwa, Department of Pharmacology, Gifu University, School of Medicine, Gifu 500-8705, Japan.
mniwa@cc.gifu-u.ac.jp
SOURCE: Life Sciences, (26 Nov 1999) 66/1 (PL-7-PL-12).
Refs: 13
ISSN: 0024-3205 CODEN: LIFSAK
PUBLISHER IDENT.: S 0024-3205(99)00566-4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
030 Pharmacology
LANGUAGE: English

SUMMARY LANGUAGE: English
AB We have shown that Hsp20, one of small molecular weight **heat shock protein**, which is present at a high concentration both in vascular smooth muscle cells and in circulating blood in patient with **vascular disease**, strongly inhibits platelet aggregation in vitro and ex vivo. To clarify the mechanism, we investigated the effect of Hsp20 on free calcium concentration in human platelet cytoplasm using fura 2. Hsp20 inhibited thrombin-induced calcium influx without affecting calcium release from intracellular calcium stores. The degree of inhibition is well-correlated with that of suppression of thrombin-induced platelet aggregation by this substance. Hsp20 also inhibited the elevation of cytoplasmic free calcium level triggered by collagen, but not that by A-23187. In contrast, Hsp28, another type of small molecular weight Hsp, failed to affect the cytoplasmic free calcium level. These findings suggest that Hsp20 inhibits the receptor-mediated calcium influx of platelets without affecting calcium release from intracellular calcium stores, leading to its anti-platelet activity.

L60 ANSWER 39 OF 90 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000010777 ESBIOBASE
TITLE: Small molecular weight heat shock-related protein, Hsp20, exhibits an anti-platelet activity by inhibiting receptor-mediated calcium influx
AUTHOR: Niwa M.; Kozawa O.; Matsuno H.; Kato K.; Uematsu T.
CORPORATE SOURCE: Dr. M. Niwa, Department of Pharmacology, Gifu University, School of Medicine, Gifu 500-8705, Japan. E-mail: mniwa@cc.gifu-u.ac.jp
SOURCE: Life Sciences, (26 NOV 1999), 66/1 (PL-7-PL-12), 13 reference(s)
CODEN: LIFSAK ISSN: 0024-3205
PUBLISHER ITEM IDENT.: S0024320599005664
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have shown that Hsp20, one of small molecular weight **heat shock protein**, which is present at a high concentration both in vascular smooth muscle cells and in circulating blood in patient with **vascular disease**, strongly inhibits platelet aggregation in vitro and ex vivo. To clarify the mechanism, we investigated the effect of Hsp20 on free calcium concentration in human platelet cytoplasm using fura 2. Hsp20 inhibited thrombin-induced calcium influx without affecting calcium release from intracellular calcium stores. The degree of inhibition is well-correlated with that of suppression of thrombin-induced platelet aggregation by this substance. Hsp20 also inhibited the elevation of cytoplasmic free calcium level triggered by collagen, but not that by A-23187. In contrast, Hsp28, another type of small molecular weight Hsp, failed to affect the cytoplasmic free calcium level. These findings suggest that Hsp20 inhibits the receptor-mediated calcium influx of platelets without affecting calcium release from intracellular calcium stores, leading to its anti-platelet activity.

L60 ANSWER 40 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:82629 BIOSIS
DOCUMENT NUMBER: PREV200000082629
TITLE: Small molecular weight heat shock-related protein, HSP20, exhibits an anti-plateletactivity by inhibiting receptor-mediated calcium influx.
AUTHOR(S): Niwa, Masayuki (1); Kozawa, Osamu; Matsuno, Hiroyuki; Kato, Kanefusa; Uematsu, Toshihiko
CORPORATE SOURCE: (1) Department of Pharmacology, Gifu University School of Medicine, Gifu, 500-8705 Japan

SOURCE: Life Sciences, (Nov. 26, 2000) Vol. 66, No. 1, pp. PL.7-PL.12.
ISSN: 0024-3205.
DOCUMENT TYPE: Article; Letter
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have shown that Hsp20, one of small molecular weight **heat shock protein**, which is present at a high concentration both in vascular smooth muscle cells and in circulating blood in patient with **vascular disease**, strongly inhibits platelet aggregation in vitro and ex vivo. To clarify the mechanism, we investigated the effect of Hsp20 on free calcium concentration in human platelet cytoplasm using fura 2. Hsp20 inhibited thrombin-induced calcium influx without affecting calcium release from intracellular calcium stores. The degree of inhibition is well-correlated with that of suppression of thrombin-induced platelet aggregation by this substance. Hsp20 also inhibited the elevation of cytoplasmic free calcium level triggered by collagen, but not that by A-23187. In contrast, Hsp28, another type of small molecular weight Hsp, failed to affect the cytoplasmic free calcium level. These findings suggest that Hsp20 inhibits the receptor-mediated calcium influx of platelets without affecting calcium release from intracellular calcium stores, leading to its anti-platelet activity.

L60 ANSWER 41 OF 90 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814

GB 1998-17943 A 19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L60 ANSWER 42 OF 90 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330929	AA	19991216	CA 1999-2330929	19990604
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
GB 2339200	B2	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-12098 A 19980606

GB	1998-28289	A	19981223
GB	1998-16086	A	19980724
GB	1998-16921	A	19980805
GB	1998-17097	A	19980807
GB	1998-17200	A	19980808
GB	1998-17632	A	19980814
GB	1998-17943	A	19980819
WO	1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L60 ANSWER 43 OF 90 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 19

ACCESSION NUMBER: 1999417165 EMBASE
TITLE: Anti-heat-shock protein 70 kDa antibodies in vascular patients.
AUTHOR: Chan Y.C.; Shukla N.; Abdus-Samee M.; Berwanger C.S.; Standord J.; Singh M; Mansfield A.O.; Stansby G.
CORPORATE SOURCE: G. Stansby, Academic Surgical Unit, 10th Floor QEQM Building, Imperial Coll. Sch. Med. St. Mary's, Praed Street, London W2 1NY, United Kingdom
SOURCE: European Journal of Vascular and Endovascular Surgery, (1999) 18/5 (381-385).
Refs: 41
ISSN: 1078-5884 CODEN: EJVSFZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Introduction and aim of study: there is recent evidence that the immune system plays an essential role in the pathogenesis of atherosclerosis, with both cellular and humoral mechanisms being involved. **Heat-shock proteins** (HSPs) have been detected in atherosclerotic lesions, and antibodies to HSPs have also been found to be raised in patients with carotid stenoses. The aim of our study was to examine the level of anti-HSP70 antibodies in patients with other **vascular diseases**. Materials and methods: a questionnaire was designed for the subjects in the study, with documentation of clinical details and ankle-brachial pressure index. Patients with concomitant infection, malignancy, hepatorenal failure, or recent surgery were excluded. Enzyme-linked immunosorbent assay (ELISA) was used to identify anti-HSP70 antibodies in the sera in different dilutions. Graphs of optical density (OD) vs. negative log dilution were plotted, the gradient of which was taken to be the estimated optical density for each subject (proportional to antibody level). Our groups consisted of controls (n = 21, mean age 59.0 .+-. 19.2), lower limb claudicants (n = 19, mean age 60.0 .+-. 12.6), patients with lower-limb critical ischaemia (n = 22, mean age 68.5 .+-. 10.07), and patients with

abdominal aortic aneurysms ((n = 20, mean age 69.9 .+-. 6.2). Results: we found no correlation between age and the estimated OD in our subjects (Spearman's correlation coefficient (r) = 0.123, one-tailed p value was 0.135). Patients with intermittent claudication, critical lower limb ischaemia, and aneurysms had higher estimated OD, and therefore higher anti-HSP70 antibody levels, than controls (Mann-Whitney test; p = 0.0127, 0.0037, 0.0008, respectively). Conclusions: our data provide the first evidence of a correlation between anti-HSP70 antibodies and different types of **vascular diseases**, suggesting that HSP70 might be involved in the pathogenesis and propagation of atherosclerosis. Since the immune response to HSPs can be modulated, this opens up the possibility of new therapeutic approaches.

L60 ANSWER 44 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:155504 BIOSIS
DOCUMENT NUMBER: PREV200000155504
TITLE: Circulating **heat shock proteins** and **heat shock protein** antibodies in peripheral **vascular disease** .
AUTHOR(S): Wright, B. H. (1); Corton, J. M. (1); Wood, R. F. M. (1); Pockley, A. G. (1)
CORPORATE SOURCE: (1) Clinical Sciences Centre, Northern General Hospital, Herries Road, Sheffield, S5 7AU UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 173. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L60 ANSWER 45 OF 90 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN DUPLICATE 20
ACCESSION NUMBER: 1999:986143 SCISEARCH
THE GENUINE ARTICLE: 265TU
TITLE: Small molecular weight heat shock-related protein, HSP20, exhibits an anti-platelet activity by inhibiting receptor-mediated calcium influx
AUTHOR: Niwa M (Reprint); Kozawa O; Matsuno H; Kato K; Uematsu T
CORPORATE SOURCE: GIFU UNIV, SCH MED, DEPT PHARMACOL, GIFU 5008705, JAPAN (Reprint); AICHI HUMAN SERV CTR, DEPT BIOCHEM, INST DEV RES, KASUGAI, AICHI 4800392, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: LIFE SCIENCES, (26 NOV 1999) Vol. 66, No. 1, pp. PL7-PL12. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0024-3205.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 13
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have shown that Hsp20, one of small molecular weight **heat shock protein**, which is present at a high concentration both in vascular smooth muscle cells and in circulating blood in patient with **vascular disease**, strongly inhibits platelet aggregation in vitro and ex vivo. To clarify the mechanism, we investigated the effect of Hsp20 on free calcium concentration in human platelet cytoplasm using fura 2. Hsp20 inhibited thrombin-induced calcium influx without affecting calcium release from intracellular calcium stores. The degree of inhibition is well-correlated with that of suppression of thrombin-induced platelet aggregation by this substance. Hsp20 also inhibited the elevation of cytoplasmic free calcium level

triggered by collagen, but not that by A-23187. In contrast, Hsp28, another type of small molecular weight Hsp, failed to affect the cytoplasmic free calcium level. These findings suggest that Hsp20 inhibits the receptor-mediated calcium influx of platelets without affecting calcium release from intracellular calcium stores, leading to its anti-platelet activity. (C) 1999 Elsevier Science Inc.

L60 ANSWER 46 OF 90 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-11869 DRUGU T E
TITLE: Modulation of endothelial gene expression in scleroderma by long-term epoprostenol infusion.
AUTHOR: Kahaleh B; Fan P S
LOCATION: Toledo, Ohio, USA
SOURCE: Arthritis Rheum. (42, No. 9, Suppl., S208, 1999)
CODEN: ARHEAW ISSN: 0004-3591
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 2000-11869 DRUGU T E
AB The effects of long term epoprostenol (prostacyclin) infusion on the expression of endothelial genes in 2 patients with limited scleroderma and pulmonary hypertension. Both patients had clinical response to the infusion with a decrease in mean pulmonary pressure and pulmonary **vascular disease**. An increase in the level of mRNA expression of angiotensin converting enzyme, endothelial nitric oxide synthase and prostacyclin synthase and a decrease in expression of endothelin-1, PDGF-a and ICAM-1 was seen after 6 mth therapy. No difference in TPA or **heat shock protein** mRNA expression was seen. The results suggested that epoprostenol therapy caused favorable changes in endothelial phenotype. (conference abstract: 63rd Annual Scientific Meeting of the American College of Rheumatology, Boston, Massachusetts, USA, 1999). (No EX).
ABEX (LL)

L60 ANSWER 47 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:413752 BIOSIS
DOCUMENT NUMBER: PREV199800413752
TITLE: The role of heat shock proteins in uveitis and Behcet's disease.
AUTHOR(S): Stanford, M. R. (1)
CORPORATE SOURCE: (1) Med. Eye Unit, St. Thomas' Hosp., Lambeth Palace Road, London SE1 7EH UK
SOURCE: Ohno, S. [Editor]; Aoki, K. [Editor]; Usui, M. [Editor]; Uchio, E. [Editor]. International Congress Series, (1998) No. 1158, pp. 3-6. International Congress Series; Uveitis today.
Publisher: Elsevier Science Publishers B.V. PO Box 211, Sara Burgerhartstraat 25, 1000 AE Amsterdam, The Netherlands.
Meeting Info.: Fourth International Symposium on Uveitis Yokohama, Japan October 10-14, 1997 International Uveitis Study Group
. ISSN: 0531-5131. ISBN: 0-444-82983-0.
DOCUMENT TYPE: Book; Conference
LANGUAGE: English

L60 ANSWER 48 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 21
ACCESSION NUMBER: 1998:319648 BIOSIS
DOCUMENT NUMBER: PREV199800319648
TITLE: The role of (auto-) immunity in atherogenesis.
AUTHOR(S): Metzler, Bernhard; Xu, Qingbo; Wick, Georg (1)
CORPORATE SOURCE: (1) Inst. Biomed. Aging Res., Austrian Acad. Sci., Rennweg

10, A-6020 Innsbruck Austria
SOURCE: Wiener Klinische Wochenschrift, (May 22, 1998) Vol. 110, No. 10, pp. 350-355.
ISSN: 0043-5325.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English; German
AB Recent data from different laboratories have provided evidence that the first stages of atherosclerosis are inflammatory in nature. Research in the last decades on this multifactorial disease has primarily focussed on the role of lipids,with only a few anectodal findings suggesting the involvement of the immune system in atherogenesis. Within the group of antigens that may be responsible for this immunoactivation during atherogenesis, **heat shock protein** (hsp) 65/60 became a serious candidate based on the fact that immunization of normocholesterolemic rabbits with **hsp65** leads to the development of arteriosclerotic lesions in the aortic intima and these primary inflammatory lesions are aggravated by a cholesterol-rich diet, thus completely resembling human fatty streaks and atherosclerotic plaques. Furthermore, T cells in atherosclerotic lesions of rabbits have been shown to react specifically with mycobacterial **hsp65**, suggesting that cell-mediated immune responses to **hsp60** are also involved in the pathogenesis of this disease. In a large epidemiological study we demonstrated that serum antibodies to mycobacterial **hsp65** were significantly increased in clinically healthy subjects with sonographically demonstrable carotid atherosclerosis. These antibodies crossreact with human **hsp60**. Thus, further elucidation of the role of the immune system in atherogenesis could enhance our understanding of the mechanism of this **vascular disorder**, and may lead to new therapeutic strategies for atherosclerosis.

L60 ANSWER 49 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 22
ACCESSION NUMBER: 1998:78130 BIOSIS
DOCUMENT NUMBER: PREV199800078130
TITLE: Inflammatory mediators are perpetuated in macrophages resistant to apoptosis induced by hypoxia.
AUTHOR(S): Yun, Jong K.; McCormick, Thomas S.; Villabona, Claudia; Judware, Raymond R.; Espinosa, Maria B.; Lapetina, Eduardo G. (1)
CORPORATE SOURCE: (1) Sch. Med., Case Western Reserve Univ., 10900 Euclid Ave., Cleveland, OH 44106-4958 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (Dec. 9, 1997) Vol. 94, No. 25, pp. 13903-13908.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A hypoxic/anoxic microenvironment has been proposed to exist within a vascular lesion due to intimal or medial cell proliferation in **vascular diseases**. Here, we examined whether hypoxia alters macrophage function by exposing murine macrophage-like RAW 264.7 (RAW) cells to hypoxia (2% O2). When cells were exposed to hypoxia, a significant number of RAW cells underwent apoptosis. Additionally, small subpopulations of RAW cells were resistant to hypoxia-induced apoptosis. Through repeated cycles of hypoxia exposure, hypoxia-induced apoptosis-resistant macrophages (HARMs) were selected; HARM cells demonstrate >70% resistance to hypoxia-induced apoptosis, as compared with the parental RAW cells. When **heat shock protein** (HSP) expression was examined after hypoxia, we observed a significant decrease in constitutive **heat shock protein** 70 (HSC 70) in RAW cells, but not in HARMs, as compared with the control normoxic condition (21% O2). In contrast, the expression level of glucose-regulated protein 78 (GRP 78) in RAW and HARM cells after hypoxia treatment was not altered, suggesting that HSC 70 and not GRP 78

may play a role in protection against hypoxia-induced apoptosis. When tumor necrosis factor a (TNF-alpha) production was examined after hypoxic treatment, a significant increase in TNF-alpha production in HARM but decrease in RAW was observed, as compared with cells cultured in normoxic conditions. HARM cells also exhibit a much lower level of modified-LDL uptake than do RAW cells, suggesting that HARMs may not transform into foam cells. These results suggest that a selective population of macrophages may adapt to potentially pathological hypoxic conditions by overcoming the apoptotic signal.

L60 ANSWER 50 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:89858 BIOSIS
DOCUMENT NUMBER: PREV199800089858
TITLE: Heat shock protein 70 synthesis of cardiac fibroblasts from fetal pigs.
AUTHOR(S): Huang, Hsiu-Chin; Lee, Wen-Chuan; Chen, Heuy-Chin; Mao, Simon J. T.; Yang, Ping-Cheng
SOURCE: Journal of the Chinese Society of Veterinary Science, (Aug., 1997) Vol. 23, No. 4, pp. 341-349. ISSN: 0253-9179.
DOCUMENT TYPE: Article
LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English
AB The purpose of this study was to characterize protein synthesis of cardiac fibroblasts from fetal pigs after heat treatments. There was no significant difference in trend of growth curves between fetal pig cardiac fibroblasts subcultured for various pas- sage numbers. Western blot analysis showed no significant difference in the expression level of desmin and vimentin among the different passages. Further studies of protein synthesis in fetal pig cardiac fibroblasts were followed by 45degree C for 60 min heat treatment. After treatments, cells were recovered for up to 12 hr and then metabolically labeled with (35S) methionine for 1 hr. De novo protein synthesis was monitored by sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE) and autoradiography. The 70 kD **heat shock protein** (HSP70) was quantitated by Western blotting using anti-HSP70 antibody. The results showed that the synthesis of HSP70 was heat-inducible and peaked at the period of 4 to 6 hr after recovery. Moreover, HSP70 was accumulated to a maximal level after 10 hr recovery. Thus, the fetal pig cardiac fibroblast cultures we established are of high purity, stability, and able to respond to heat shock treatment. This in vitro model may provide a valuable tool for the study of heat shock response played in cardiac-**vascular diseases**.

L60 ANSWER 51 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 23
ACCESSION NUMBER: 1998:116507 BIOSIS
DOCUMENT NUMBER: PREV199800116507
TITLE: Effect of combined heat, ozonation and ultraviolet irradiation (VasoCare) on heat shock protein expression by peripheral blood leukocyte populations.
AUTHOR(S): Bulmer, J.; Bolton, A. E.; Pockley, A. G. (1)
CORPORATE SOURCE: (1) Div. Clin. Sci., Clin. Sci. Cent., Northern General Hosp., Herries Rd., Sheffield S5 7AU UK
SOURCE: Journal of Biological Regulators and Homeostatic Agents, (July-Sept., 1997) Vol. 11, No. 3, pp. 104-110. ISSN: 0393-974X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The re-administration of whole blood subjected to heat, ozonation and ultraviolet irradiation (VasoCare therapy) has been shown to elicit clinical benefits in individuals with **vascular disease**. Given that these stressors induce **heat shock protein** (Hsp) expression and that **heat shock protein** reactivity is implicated in the pathogenesis of

vascular disease, this study assessed the effect of VasoCare on intracellular expression of **Hsp60** and Hsp 70 by treated peripheral blood leukocytes. Contrary to expectations, VasoCare induced a significant reduction (apprx 40%) in the proportion of peripheral blood mononuclear cells expressing intracellular **Hsp60** and Hsp70, whereas it had no effect on **heat shock protein** expression by peripheral blood neutrophils. Cell surface **heat shock protein** expression was not detectable. The reduced expression of **Hsp60** by mononuclear cells was concomitant with an increase in the levels of **Hsp60** in treated plasma. Although the mechanism underlying the clinical effectiveness of VasoCare therapy has yet to be established, it may be that re-administration of treated blood or soluble factors derived there from modifies in vivo immune responsiveness to **heat shock proteins** or associated molecules.

L60 ANSWER 52 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 24
ACCESSION NUMBER: 1996:317005 BIOSIS
DOCUMENT NUMBER: PREV199699039361
TITLE: Increased antibody titers against mycobacterial heat-shock protein 65 in patients with vasculitis and arteriosclerosis.
AUTHOR(S): Gruber, R. (1); Lederer, S.; Bechtel, U.; Lob, S.; Riethmueller, G.; Feucht, H. E.
CORPORATE SOURCE: (1) Inst. Immunol., Univ. Muenchen, Goethestrasse 31, D-80336 Muenchen Germany
SOURCE: International Archives of Allergy and Immunology, (1996) Vol. 110, No. 1, pp. 95-98.
ISSN: 1018-2438.
DOCUMENT TYPE: Article
LANGUAGE: English
AB **Heat shock proteins** (HSPs) are a group of highly conserved proteins that show extensive homology at the DNA and protein level among bacterial and mammalian species. Furthermore, bacterial HSPs induce specific cellular and humoral immune responses in mammals. Cross-reacting antibodies may therefore be induced in chronic infections. Recently, it has been claimed that patients with arteriosclerosis (AS) of the carotid arteries have significantly elevated antibody titers to mycobacterial HSPs. In this study, we extended the spectrum of **vascular diseases** and analyzed sera from patients with systemic vasculitis and systemic lupus erythematosus (SLE) for the presence of anti-HSP antibodies. Anti-HSP antibodies, tested in an ELISA with recombinant mycobacterial HSP 65, were significantly elevated in patients with vasculitis (n = 56; p lt 0.01) and AS (n = 29; p lt 0.0001), but only marginally in patients with SLE (n = 22; p gt 0.05) compared to healthy controls (n = 90). These findings further support the concept of infection-induced immune reactions playing a pathogenic role in the development of both AS and vasculitis.

L60 ANSWER 53 OF 90 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 25
ACCESSION NUMBER: 1995:449548 BIOSIS
DOCUMENT NUMBER: PREV199598463848
TITLE: Acute Hypertension Induces Heat-Shock Protein 70 Gene Expression in Rat Aorta.
AUTHOR(S): Xu, Qingbo (1); Li, Ding-Gang; Holbrook, Nikki J.; Udelsman, Robert
CORPORATE SOURCE: (1) Sect. Gene Expression Aging, Natl. Inst. Aging, Natl. Inst. Health, 4940 Eastern Ave., Baltimore, MD 21224 USA
SOURCE: Circulation, (1995) Vol. 92, No. 5, pp. 1223-1229.
ISSN: 0009-7322.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Background: Many factors cause acute systemic hypertension, which in turn

can result in damage to the vessel wall and lead to **vascular disease**. In previous studies, we demonstrated that restraint, or immobilization stress, results in the induction of **heat-shock protein** 70 (hsp70) gene expression in the aorta of adult rat and showed that this response was markedly attenuated with age. Methods and Results: Here we provide evidence that restraint-induced hsp70 expression occurs secondary to a rise in systemic blood pressure. Old rats were unable to mount a significant stress-induced hypertensive response, providing an explanation for the reduced hsp70 response in the old rats. A variety of vasoactive agents that induce acute hypertension through distinct signal transduction pathways, including phenylephrine, dopamine, vasopressin, angiotensin II, and endothelin-1, were found to result in hsp70 mRNA induction in the aorta. The magnitude of hsp70 expression achieved with these hypertensive agents was directly correlated with their relative effects on blood pressure. Rats were treated with the vasodilator sodium nitroprusside, which prevented an acute rise in blood pressure from the hypertensive agents tested and abolished induction of hsp70 expression. Conclusions: These findings support the conclusion that hsp70 induction occurs as a physiological response to acute hypertension and suggest the possibility that hsp70 plays a role in the protecting the vasculature from damage during hemodynamic stress.

L60 ANSWER 54 OF 90 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 26

ACCESSION NUMBER: 1995-0576494 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Atherosclerosis as an autoimmune condition
AUTHOR: KLEINDIENST R.; SCHETT G.; AMBERGER A.; SEITZ C. S.; MICHAELIS D.; METZLER B.; DIETRICH H.; QINGBO XU; WICK G.
CORPORATE SOURCE: Austrian acad. sci., inst. biomedical aging res., 6020 Innsbruck, Austria
SOURCE: Israel journal of medical sciences, (1995), 31(10), 596-599, 26 refs.
ISSN: 0021-2180 CODEN: IJMDAI
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Israel
LANGUAGE: English
AVAILABILITY: INIST-1821, 354000050257480020

AN 1995-0576494 PASCAL
CP Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
AB Atherosclerosis is a multifactorial **vascular disorder** responsible for the highest rate of mortality in the western world. During the last decades, research on this disease has primarily focused on the role of lipids, which are essential to the formation of lesions in the vascular intima that ultimately leads to clinically apparent atherosclerotic plaques. More recently, several anecdotal findings have indicated the possible involvement of the immune system in the process of atherogenesis. In particular, the appearance of immunocompetent cells as well as humoral antibodies in the intima in the early stages of disease development supports the view of an inflammatory component in this disorder. In addition to the search for lipid-associated antigens that might entail full-blown atherosclerosis, other candidate antigens capable of inducing an immune response in the vascular wall have also been explored. Within the probable group of antigens for immune responsiveness, **heat shock protein** (hsp) 60/65 became a serious candidate, upon observation that immunization of rabbits with this protein led to arteriosclerotic changes of the aortic intima. In the last few years we have established this rabbit model for immunologic investigations of atherosclerosis and, in parallel, examined the pathogenesis of human atherosclerosis with regard to hsp 60/65 immune reactivity. Currently available data point to an autoimmune induction of early inflammatory arteriosclerotic changes triggered by a cellular and

humoral immune reaction to stress-induced hsp 60-expressing areas of the endothelial cells.

L60 ANSWER 55 OF 90 JICST-EPlus COPYRIGHT 2003 JST on STN
ACCESSION NUMBER: 950289572 JICST-EPlus
TITLE: Role of **heat shock proteins** in **vascular disorder**.
AUTHOR: MINODA SEIJI
CORPORATE SOURCE: Jichi Med. Sch.
SOURCE: Bio Clin, (1995) vol. 10, no. 4, pp. 285-288. Journal Code: L0059A (Fig. 1, Tbl. 1, Ref. 9)
ISSN: 0919-8237
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New

L60 ANSWER 56 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73455 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human cyclophilin-40 (CYP) tetratricopeptide repeat 2 (TPR2) motif.
AN ABG73455 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human cyclophilin-40 (CYP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 57 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73454 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human protein phosphatase 5 tetratricopeptide repeat 3 (TPR3) motif.

AN ABG73454 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human protein phosphatase 5 (PP5) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 58 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73453 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human protein phosphatase 5 tetratricopeptide repeat 2 (TPR2) motif.

AN ABG73453 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human protein phosphatase 5 (PP5) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 59 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73452 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an

inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human Hsc70-interacting protein tetratricopeptide repeat 3 (TPR3) motif.

AN ABG73452 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human Hsc70-interacting protein (HIP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 60 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73451 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human Hsc70-interacting protein tetratricopeptide repeat 2 (TPR2) motif.

AN ABG73451 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This

sequence represents a human Hsc70-interacting protein (HIP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 61 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73450 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human cyclophilin-40 (CYP) tetratricopeptide repeat 3 (TPR3) motif.
AN ABG73450 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human cyclophilin-40 (CYP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 62 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73449 Protein DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Carboxyl terminus of Hsc70-interacting protein (CHIP) consensus sequence.
AN ABG73449 Protein DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when

the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a CHIP polypeptide consensus sequence used in the exemplification of the invention.

L60 ANSWER 63 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73448 Protein DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: N-PSDB: ABX12286
DESCRIPTION: Drosophila carboxyl terminus of Hsc70-interacting protein (CHIP).
AN ABG73448 Protein DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents the Drosophila CHIP polypeptide of the invention.

L60 ANSWER 64 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73447 Protein DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: N-PSDB: ABX12285
DESCRIPTION: Mouse carboxyl terminus of Hsc70-interacting protein (CHIP).
AN ABG73447 Protein DGENE

AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents the mouse CHIP polypeptide of the invention.

L60 ANSWER 65 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73446 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Tetratricopeptide repeat (TPR) domain consensus sequence.
AN ABG73446 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a tetratricopeptide repeat domain consensus sequence, used in the exemplification of the invention.

L60 ANSWER 66 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73445 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human cyclophilin-40 (CYP) tetratricopeptide repeat 1 (TPR1) motif.

AN ABG73445 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human cyclophilin-40 (CYP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 67 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73444 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human protein phosphatase 5 tetratricopeptide repeat 1 (TPR1) motif.

AN ABG73444 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human protein phosphatase 5 (PP5) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 68 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73443 Peptide DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -

INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human Hsc70-interacting protein tetratricopeptide repeat 1 (TPR1) motif.

AN ABG73443 Peptide DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a human Hsc70-interacting protein (HIP) tetratricopeptide repeat motif, used in the exemplification of the invention.

L60 ANSWER 69 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABG73442 Protein DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: N-PSDB: ABX12284; ABX12287
DESCRIPTION: Human carboxyl terminus of Hsc70-interacting protein (CHIP).

AN ABG73442 Protein DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents the human CHIP polypeptide of the invention.

L60 ANSWER 70 OF 90 DGENE' COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11757 Protein DGENE
TITLE: Treating a **vascular disorder**, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Chlamydophila pneumoniae heat shock protein 60 (HSP60).
AN AAE11757 Protein DGENE
AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory disorder, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss disease), Cogan's syndrome, graft-versus-host disease (GvHD), Henoch-Schonlein purpura, Kawasaki disease, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's disease). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 60 (**HSP60**) from Chlamydophila pneumoniae.

L60 ANSWER 71 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11756 Protein DGENE
TITLE: Treating a **vascular disorder**, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Human heat shock protein 60 (HSP60).
AN AAE11756 Protein DGENE
AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory disorder, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss disease), Cogan's syndrome,

graft-versus-host disease (GvHD), Henoch-Schonlein purpura, Kawasaki disease, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's disease). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 60 (**HSP60**) from human.

L60 ANSWER 72 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAE11755 Protein DGENE
TITLE: Treating a **vascular disorder**, involves administering a composition comprising **heat shock protein**, its fragment or analog, by mucosal surface, pulmonary tract, oral or enteral route, or by inhalation -
INVENTOR: Weiner H L; Maron R; Libby P
PATENT ASSIGNEE: (BGHM)BRIGHAM & WOMENS HOSPITAL INC.
PATENT INFO: WO 2001068124 A2 20010920 49p
APPLICATION INFO: WO 2001-US8351 20010315
PRIORITY INFO: US 2000-189855P 20000315
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2001-611383 [70]
DESCRIPTION: Mycobacterium tuberculosis heat shock protein 65 (HSP65).
AN AAE11755 Protein DGENE
AB The patent discloses methods for treating **vascular disorders** in mammals. The method involves administering a composition comprising at least one agent selected from **heat shock protein** (HSP), its fragment or analogue, through mucosal surface, pulmonary tract, oral or enteral route or by inhalation. Compositions comprising HSP are useful for treating and suppressing a **vascular disorder**, including cell-mediated immune response, an antibody-mediated immune response, cell-mediated inflammatory disorder, atherosclerosis, allergic angiitis, Behcet's syndrome, granulomatosis (Churg-Strauss disease), Cogan's syndrome, graft-versus-host disease (GvHD), Henoch-Schonlein purpura, Kawasaki disease, leucocytoclastic vasculitis, polyarteritis nodosa (PAN), microscopic polyangiitis, polyangiitis overlap syndrome, Takayasu's arteritis, temporal arteritis, transplant rejection, Wegener's granulomatosis and thromboangiitis obliterans (Buerger's disease). They are useful for reducing the level of proinflammatory Th1 cytokines and also for increasing the level of antiinflammatory Th2 cytokines. The present sequence is **heat shock protein** 65 (**HSP65**) from Mycobacterium tuberculosis.

L60 ANSWER 73 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAB09886 protein DGENE
TITLE: Intracellular targeted delivery of compounds using the 70 kiloDalton heat shock protein, useful in the treatment of transplant rejection, autoimmune diseases and cancer -
INVENTOR: Fujihara S M; Nadler S G
PATENT ASSIGNEE: (BRIM)BRISTOL-MYERS SQUIBB CO.
PATENT INFO: WO 2000031113 A1 20000602 37p
APPLICATION INFO: WO 1999-US27244 19991117
PRIORITY INFO: US 1998-109872 19981124
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-400029 [34]
DESCRIPTION: Hsp70 C-terminal 244 amino acid polypeptide sequence.
AN AAB09886 protein DGENE
AB The present sequence is the C-terminal 244 amino acids of the 70kD **heat shock protein** (Hsp70). This sequence was used in a fusion protein with the p50 subunit of transcription factor

NF-kappaB, the sequence of which is indicated in the specification as being SEQ ID NO: 1, but which is not given. This fusion protein was created in order to determine the ability of the Hsp70 sequence to direct other proteins into the cell. It was shown that Hsp70 fragments are able to direct other proteins into the cell, a feature which can be used in the treatment of transplant rejection, autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, diabetes, asthma, inflammatory bowel disease, psoriasis, hepatitis, Graves' disease and viteligo, inflammatory diseases including osteoarthritis, pancreatitis and adult respiratory distress syndrome, cancer, **vascular diseases** (such as restenosis and atherosclerosis) and DNA and RNA viral replication diseases (including herpes).

L60 ANSWER 74 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAB09885 protein DGENE
TITLE: Intracellular targeted delivery of compounds using the 70 kiloDalton heat shock protein, useful in the treatment of transplant rejection, autoimmune diseases and cancer -
INVENTOR: Fujihara S M; Nadler S G
PATENT ASSIGNEE: (BRIM) BRISTOL-MYERS SQUIBB CO.
PATENT INFO: WO 2000031113 A1 20000602 37p
APPLICATION INFO: WO 1999-US27244 19991117
PRIORITY INFO: US 1998-109872 19981124
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-400029 [34]
DESCRIPTION: Hsp70 C-terminal 92 amino acid polypeptide sequence.
AN AAB09885 protein DGENE
AB The present sequence is the C-terminal 92 amino acids of the 70kD **heat shock protein** (Hsp70). This sequence was used in a fusion protein with the p50 subunit of transcription factor NF-kappaB, the sequence of which is indicated in the specification as being SEQ ID NO: 1, but which is not given. This fusion protein was created in order to determine the ability of the Hsp70 sequence to direct other proteins into the cell. It was shown that Hsp70 fragments are able to direct other proteins into the cell, a feature which can be used in the treatment of transplant rejection, autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, diabetes, asthma, inflammatory bowel disease, psoriasis, hepatitis, Graves' disease and viteligo, inflammatory diseases including osteoarthritis, pancreatitis and adult respiratory distress syndrome, cancer, **vascular diseases** (such as restenosis and atherosclerosis) and DNA and RNA viral replication diseases (including herpes).

L60 ANSWER 75 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABX12289 DNA DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human expressed sequence tag (EST) PCR primer #2.
AN ABX12289 DNA DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein

is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a PCR primer used in the exemplification of the invention.

L60 ANSWER 76 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABX12288 DNA DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
DESCRIPTION: Human expressed sequence tag (EST) PCR primer #1.
AN ABX12288 DNA DGENE
AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents a PCR primer used in the exemplification of the invention.

L60 ANSWER 77 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABX12287 DNA DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: P-PSDB: ABG73442

DESCRIPTION: Human carboxyl terminus of Hsc70-interacting protein (CHIP) genomic DNA.

AN ABX12287 DNA DGENE

AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents genomic DNA encoding the human CHIP polypeptide of the invention.

L60 ANSWER 78 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: ABX12286 cDNA DGENE

TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -

INVENTOR: Patterson W C; Ballinger C A

PATENT ASSIGNEE: (TEXA) UNIV TEXAS SYSTEM.

PATENT INFO: US 2002177212 A1 20021128 50p

APPLICATION INFO: US 2001-13939 20011207

PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2003-298777 [29]

CROSS REFERENCES: P-PSDB: ABG73448

DESCRIPTION: Drosophila carboxyl terminus of Hsc70-interacting protein (CHIP) cDNA.

AN ABX12286 cDNA DGENE

AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents cDNA encoding the Drosophila CHIP polypeptide of the invention.

L60 ANSWER 79 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: ABX12285 cDNA DGENE

TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -

INVENTOR: Patterson W C; Ballinger C A

PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: P-PSDB: ABG73447
DESCRIPTION: Mouse carboxyl terminus of Hsc70-interacting protein (CHIP) cDNA.

AN ABX12285 cDNA DGENE

AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents cDNA encoding the mouse CHIP polypeptide of the invention.

L60 ANSWER 80 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: ABX12284 cDNA DGENE
TITLE: New polypeptide which negatively regulates binding of heat shock protein to a substrate or induces ubiquitylation of a heat shock bound substrate, useful for identifying an inhibitor of the polypeptide -
INVENTOR: Patterson W C; Ballinger C A
PATENT ASSIGNEE: (TEXA)UNIV TEXAS SYSTEM.
PATENT INFO: US 2002177212 A1 20021128 50p
APPLICATION INFO: US 2001-13939 20011207
PRIORITY INFO: US 1999-134433P 19990517
US 2000-573473 20000517
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2003-298777 [29]
CROSS REFERENCES: P-PSDB: ABG73442
DESCRIPTION: Human carboxyl terminus of Hsc70-interacting protein (CHIP) cDNA.

AN ABX12284 cDNA DGENE

AB The invention relates to a carboxyl terminus of Hsc70-interacting protein (CHIP) which negatively regulates binding of **heat shock protein** (Hsp), such as Hsc70, Hsp70 or Hsc90, to a substrate or induces ubiquitylation of a heat shock bound substrate. The CHIP protein is useful for identifying an inhibitor of CHIP by incubating the CHIP protein with a compound under conditions that promote the negative regulating activity or ubiquitylation activity of the polypeptide when the compound is not present, and determining if the negative regulating activity or ubiquitylation activity of the polypeptide is reduced relative to the negative regulating activity or ubiquitylation activity of the polypeptide in the absence of the compound. The CHIP protein is useful treating, inhibiting or preventing neoplastic diseases such as cancer and lymphoma, ischaemic diseases such as stroke, **vascular diseases**, myocardial infarction and diseases characterised by inflammation which include infections and autoimmune diseases. This sequence represents cDNA encoding the human CHIP polypeptide of the

invention.

L60 ANSWER 81 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAA61056 DNA DGENE
TITLE: Intracellular targeted delivery of compounds using the 70 kiloDalton heat shock protein, useful in the treatment of transplant rejection, autoimmune diseases and cancer -
INVENTOR: Fujihara S M; Nadler S G
PATENT ASSIGNEE: (BRIM) BRISTOL-MYERS SQUIBB CO.
PATENT INFO: WO 2000031113 A1 20000602 37p
APPLICATION INFO: WO 1999-US27244 19991117
PRIORITY INFO: US 1998-109872 19981124
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-400029 [34]
DESCRIPTION: Electrophoretic mobility shift assay protein concentration primer #2.
AN AAA61056 DNA DGENE
AB The present sequence is a primer which was used to determine the concentration of a fusion protein in an electrophoretic mobility shift assay. The fusion protein comprised the C-terminuus of the 70kD **heat shock protein** (Hsp70), and the p50 subunit of transcription factor NF-kappaB. The fusion protein was created in order to determine the ability of the Hsp70 sequence to direct other proteins into the cell. It was shown that Hsp70 fragments are able to direct other proteins into the cell, a feature which can be used in the treatment of transplant rejection, autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, diabetes, asthma, inflammatory bowel disease, psoriasis, hepatitis, Graves' disease and viteligo, inflammatory diseases including osteoarthritis, pancreatitis and adult respiratory distress syndrome, cancer, **vascular diseases** (such as restenosis and atherosclerosis) and DNA and RNA viral replication diseases (including herpes).

L60 ANSWER 82 OF 90 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: AAA61055 DNA DGENE
TITLE: Intracellular targeted delivery of compounds using the 70 kiloDalton heat shock protein, useful in the treatment of transplant rejection, autoimmune diseases and cancer -
INVENTOR: Fujihara S M; Nadler S G
PATENT ASSIGNEE: (BRIM) BRISTOL-MYERS SQUIBB CO.
PATENT INFO: WO 2000031113 A1 20000602 37p
APPLICATION INFO: WO 1999-US27244 19991117
PRIORITY INFO: US 1998-109872 19981124
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-400029 [34]
DESCRIPTION: Electrophoretic mobility shift assay protein concentration primer #1.
AN AAA61055 DNA DGENE
AB The present sequence is a primer which was used to determine the concentration of a fusion protein in an electrophoretic mobility shift assay. The fusion protein comprised the C-terminuus of the 70kD **heat shock protein** (Hsp70), and the p50 subunit of transcription factor NF-kappaB. The fusion protein was created in order to determine the ability of the Hsp70 sequence to direct other proteins into the cell. It was shown that Hsp70 fragments are able to direct other proteins into the cell, a feature which can be used in the treatment of transplant rejection, autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, diabetes, asthma, inflammatory bowel disease, psoriasis, hepatitis, Graves' disease and viteligo, inflammatory diseases including osteoarthritis, pancreatitis and adult respiratory distress syndrome, cancer, **vascular diseases** (such as restenosis and atherosclerosis) and DNA and RNA viral replication diseases (including herpes).

L60 ANSWER 83 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:196067 FEDRIP
NUMBER OF REPORT: CRISP 1Z01NS02933-06
RESEARCH TITLE: Cerebral Ischemia: Role Of Cell Mediators In Pathogenesi
STAFF: Principal Investigator: SPATZ, MARIA
SUPPORTING ORGN: Supported By: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
FISCAL YEAR: 2002
FUNDING: Not Applicable
FILE SEGMENT: National Institutes of Health
SUM I. PATHOGNESIS OF CEREBRAL ISCHEMIA: The discovery of ET-1 and NO has greatly contributed to our understanding of the functional changes of many organs under physiological and pathological conditions (e.g., hypertension, atherosclerosis, and stroke). In the brain, the endothelium is the main producer of ET-1 and NO, although both of these substances are produced by a variety of cellular elements (e.g., smooth muscle, glia, and neurons). Endothelial ET-1 was shown to induce NO secretion that, in turn, reduced the production of ET-1. These reactions, which are mediated by ETA and ETB receptors, contribute to the maintenance of vascular tone and control of circulation (e.g., cerebral blood flow and blood pressure) as well as blood-brain barrier function. The regulatory mechanisms involved in this interplay have recently been shown to involve Ca2+ mobilization, cytoskeletal (actin and vimentin) rearrangements and vasodilator-stimulated phosphoprotein changes that are mediated by c-GMP/c-GMP kinase system. Recently studies focused on interactions of endocannabinoids [2-arachidonoylglycerol (2-AG) and anandamide (ANA)] with the vasoconstrictor, endothelin-1 (ET-1). Both 2-AG and ANA are produced in various organs (brain, gut) and cells [monocytes, platelets, endothelial cells (EC)]; they elicit neuromodulatory,cytoprotective (i.e. brain ischemia and trauma)and cardiovascular effects, which are mediated through cannabinoid (CB) receptors CB1, CB2 or vanilloid (VRA1) receptors. Current research analyzes the cytoprotective properties and distinct mechanisms involved in the modulation of endothelial responses by these substances. Changes in the Ca2+ levels and the cytoskeleton rearrangements in cerebral vascular EC implicate the active participation of CB1 receptors in EC function and possibly cerebral **vascular disease** processes. These findings implicate 2-AG/ET-1 interactions in cerebral capillary and microvascular endothelial responses and provide a potential alternative pathway for abrogating ET-1-inducible microvascular effects in the brain. Most recently, we also have investigated the possible role of nitroxides in ameliorating postischemic hypoperfusion. All of these findings may prove useful in devising a multifactorial strategy for the treatment of cerebral ischemia. II. TOLERANCE TO CEREBRAL ISCHEMIA: The study of SHR-SP tolerization with E-selectin (in collaboration with Dr. J. Hallenbeck) demonstrated a reduced incidence and size of brain infarct and hemorrhage. Continued investigation is focused on the mechamism responsible for these events. In addition, a new initiative for stroke prevention (induction of mucosal tolerance to E-selectin) involves a preclinical study with spontaneously hypertensive, genetically stroke-prone rats and an approved Phase II A Clinical Trial

L60 ANSWER 84 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:189221 FEDRIP
NUMBER OF REPORT: CRISP 1R01HL72768-01
RESEARCH TITLE: BRADYKININ SIGNALING IN REGULATION OF eNOS
STAFF: Principal Investigator: VENEMA, RICHARD C; RVENEMA@MAIL.MCG.EDU, MEDICAL COLLEGE OF GEORGIA, RM #CB3212B, VASCULAR BIOL CTR
PERFORMING ORGN: MEDICAL COLLEGE OF GEORGIA, AUGUSTA, GEORGIA
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2003 (/15/03)

FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2002 (/28/07)
FUNDING: New Award (Type 1)
FILE SEGMENT: National Institutes of Health
SUM DESCRIPTION (provided by applicant): Endothelium-derived nitric oxide (NO) has a crucial role in regulation of the state of vasodilation of blood vessels and hence in regulation of blood pressure. Furthermore, because NO regulates this and a number of other important vascular processes, abnormalities in vascular NO production are thought to contribute to the pathogenesis of certain **vascular disorders** such as those of atherosclerosis, diabetes, and hypertension. NO is synthesized in endothelial cells by oxidation of L-arginine in a reaction catalyzed by the enzyme, endothelial nitric oxide synthase (eNOS). Recent investigations in several laboratories have established a role for Ser-1179 phosphorylation and Thr-497 dephosphorylation in agonist regulation of eNOS activity in endothelial cells. Data presented in the Preliminary Studies section of this proposal provide evidence for two additional sites of eNOS phosphorylation at Ser-617 and Ser-635. Our preliminary data shows that these two sites are transiently phosphorylated in cultured endothelial cells in response to stimulation with the eNOS-activating agonists bradykinin (BK), ATP, and vascular endothelial growth factor. The principal aim of the present proposal is to examine the hypothesis that eNOS activity in vascular endothelial cells is regulated in part by BK-stimulated phosphorylation of the enzyme at Ser-617 and Ser-635. Additional aims are to elucidate the molecular mechanism(s) by which phosphorylation at Ser-617 and Ser-635 alters enzyme catalytic activity and to test the hypothesis that phosphorylation at Ser-617 or Ser-635 alters eNOS protein-protein interactions with caveolin-1, the bradykinin B2 receptor, or **heat shock protein** 90. Finally, we will examine whether certain pathophysiological conditions, such as hyperglycemia or oxidative stress, alter either basal or BK-stimulated phosphorylation of eNOS at Ser-617 or Ser-635.

L60 ANSWER 85 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:188805 FEDRIP
NUMBER OF REPORT: CRISP 5R01HL71214-02
RESEARCH TITLE: Hsp90 Mediates eNOS and Vascular Function
STAFF: Principal Investigator: PRITCHARD, JR, KIRKWOOD A, JR
; KPRITCH@MCW.EDU, MEDICAL COLLEGE OF WISCONSIN, 8701 WATEROWN PLANK ROAD
PERFORMING ORGN: MEDICAL COLLEGE OF WISCONSIN, MILWAUKEE, WISCONSIN
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2008 (/01/02)
FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2007 (/31/06)
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health
SUM DESCRIPTION (provided by the applicant): The overall goal of this application is to determine the mechanisms by which **heat shock protein** 90 (Hsp90) mediates endothelial nitric oxide synthase (eNOS) function to direct endothelial biology and vascular physiology. Recent reports from this laboratory demonstrate that eNOS is fully capable of generating both nitric oxide (.NO) and superoxide anion (O2-). When conformational changes in Hsp90 are blocked with geldanamycin (GA) eNOS generates O2- upon activation. When endothelial cultures and isolated pressurized microvessels are pre-treated with angiostatin they also appear to generate O2 about by an eNOS-dependent mechanism to shift the balance from .NO towards O2 about which impairs vasodilation. These data suggest that Hsp90 interactions direct which radical species is generated by eNOS. Both angiostatin and GA induce altered states of eNOS activation as defined by the levels of phospho-eNOS (S1179) on eNOS and Hsp90 associated with eNOS. Additional studies aimed at determining the phosphorylation state of eNOS suggest that Hsp90 interactions with eNOS

may protect or promote serine phosphorylation at another site on eNOS. As the presence of phosphoserine on eNOS inversely correlates with O2 about this site may influence the function of eNOS by directing radical species generation. The signal transduction mechanisms governing Hsp90 interactions with eNOS with respect to O2 about generation remain unknown. As the balance of .NO and O2 about in the endothelium mediate many functions, endothelial proliferation and vasodilation, understanding how angiostatin and GA alter signaling pathways governing eNOS function is central to understanding the mechanisms governing angiogenesis for developing new collatoral vessels and increasing vasodilation to prevent ischemic heart disease. Findings from these studies will probably be relevant to and provide new understanding of mechanisms mediating **vascular disease** related to atherogenesis, hypertension and diabetes

L60 ANSWER 86 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:188713 FEDRIP
NUMBER OF REPORT: CRISP 5R01HL70929-02
RESEARCH TITLE: Functions and Mechanisms of Ref-1 in the Endothlium
STAFF: Principal Investigator: IRANI, KAIKOBAD J.; KIRANI@JHMI.EDU, JOHNS HOPKINS UNIV SCH OF MED, 720 RUTLAND AVE / ROSS 1023
PERFORMING ORGN: JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2008 (/01/02)
FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2007 (/31/07)
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health
SUM DESCRIPTION (provided by the applicant): Perturbations in the reduction-oxidation (redox) status of the endothelium, determined by the production and elimination of reactive oxygen species (ROS) and endothelial nitric oxide (NO), contributes to the pathogenesis of many **vascular disorders** such as atherosclerosis, restenosis, and hypertension.Redox factor-1 (ref-1) is a ubiquitous DNA repair enzyme/transcriptional regulator. If and how ref-1 affects endothelial redox status and function is not known. Based on preliminary evidence, this proposal advances the novel concept that ref-i regulates endothelial production of ROS and NO, and therefore is a crucial determinant of endothelial redox state. Proposed experiments will test the role and mechanisms of ref-1 in regulating the production of endothelial ROS and NO. The effect of ref-1 on eNOS, Akt kinase, and NAD(P)H oxidase activities, and **heat shock protein** expression, as possible mechanisms for its effects on endothelial NO and ROS generation will be explored. The domains of ref-1 that are important in regulating the activities/expression of these mediators will be characterized. In addition to defining the function(s) of ref-1 in cultured endothelial cells, adenoviral gene transfer experiments in whole vessels will also elucidate its role in regulating endothelium-derived bioavailable NO, and endothelium-dependent vascular tone. Finally, the roles of eNOS-derived NO, and ROS derived from the rac1 -regulated NAD (P) H oxidase in regulating the function, expression, and sub-cellular localization of ref-1 in the endothelium will be defined.Ref-1, as a master regulator of transcription and a DNA repair enzyme, participates in fundamental cellular processes such as proliferation, apoptosis, and differentiation. The importance of ref-1 in the cardiovascular system is only beginning to be appreciated. By investigating the regulation of ref-1 in the endothelium, its role in endothelial physiology and pathophysiology, and by examining both transcriptional and novel non-transcriptional mechanisms of action of ref-1, this proposal promises to advance our current understanding of its functions in vascular biology and disease.

L60 ANSWER 87 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN

ACCESSION NUMBER: 2003:186923 FEDRIP
NUMBER OF REPORT: CRISP 5R01HL65619-03
RESEARCH TITLE: CHIP,myocyte signaling, and the response to stress
STAFF: Principal Investigator: PATTERSON, WINSTON C.; CPATTERS@MED.UNC.EDU, UNIV OF NC AT CHAPEL HILL, 5109 NEUROSCIENCE RES BLDG
PERFORMING ORGN: UNIVERSITY OF NORTH CAROLINA CHAPEL HILL, CHAPEL HILL, NORTH CAROLINA
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2007 (/20/01)
FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2006 (/30/05)
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health
SUM The cellular response to ischemia and other forms of stress is a critical determinant of viability in the setting of **vascular disease**, and therefore affects the outcome of patients with stroke, myocardial infarction, and peripheral **vascular disease**. Cellular viability is affected in a negative fashion by stress-responsive signaling pathways that activate cell death programs and other deleterious processes, and in a positive fashion by protective responses, the most powerful and well- characterized of which are the molecular chaperones or **heat shock proteins**.
We have recently identified a novel, developmentally regulated protein called CHIP (carboxyl terminus of Hsc 70- interacting protein) that interacts with the molecular chaperones (Hsc70, Hsp70, and Hsp90) and negatively regulates their functions. We have also shown that CHIP targets a subset of cellular proteins, including NOS3, for degradation and can activate the NF-kappaB signaling pathway. We hypothesize that CHIP antagonizes the cellular effects of molecular chaperones in tissues in which it is highly expressed, such as the heart. The study of CHIP should therefore provide an excellent model to understand protective mechanisms in the setting of ischemic **vascular disease**. To test our hypotheses, we will characterize the role of **heat shock proteins** and CHIP in regulation of stress-responsive signaling pathways such as NF- kappaB and NOS3 (Aims I and II) and determine the effects of modulation of CHIP expression on the cellular stress response (apoptosis, inflammation, and hypertrophy) in cell culture (Aim III). To define the role of CHIP in myocardial ischemia, we have created mice deficient in CHIP by homologous recombination. These mice will be utilized to determine the role of CHIP in modulating the response to hypertrophy and ischemia (Aim IV). These studies should help us to understand the role of molecular chaperones and in ubiquitin-proteasome pathway in cellular protective responses in the setting of ischemia, and have the potential to identify new targets for intervention in the treatment of ischemic cardiovascular and cerebrovascular disease.

L60 ANSWER 88 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:184030 FEDRIP
NUMBER OF REPORT: CRISP 5P01HL48743-11 0007
RESEARCH TITLE: INFLAMMATORY AND INFECTIOUS MECHANISMS IN ATHEROGENESIS
STAFF: Principal Investigator: LIBBY, PETER W; BRIGHAM & WOMEN'S HOSPITAL, 221 LONGWOOD AVE
PERFORMING ORGN: BRIGHAM AND WOMEN'S HOSPITAL, BOSTON, MASSACHUSETTS
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2009 (/30/92)
FISCAL YEAR: 2002
ESTD COMPLETION DATE: 2008 (/31/04)
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health
SUM DESCRIPTION (Adapted from the applicant?s abstract) The most effective

contemporary lipid lowering regimens reduce the major manifestations of atherosclerosis by at most a third. Thus, the majority of cardiovascular events occurred despite effective management of low density lipoprotein cholesterol. Moreover, there is a wide range of expression of atherosclerotic complications in individuals with similar profiles of traditional risk factors. Also, the episodic nature of the evolution and manifestations of atherosclerosis remains unexplained by simple consideration of the systemic risk factors long implicated in atherogenesis. Considerable sero-epidemiological evidence links infectious processes with cardiovascular risk. Additionally, current thought highlights inflammatory mechanisms as major contributors to atherogenesis and in the precipitation of the clinical manifestations of atherosclerosis. Project 1 will link these disparate observations into a unifying hypothesis. We postulate that infectious agents may potentiate traditional risk factors, heightening atherogenesis and contributing to the triggering of its acute manifestations. Recent evidence has clearly localized Chlamydia pneumoniae within human atherosclerotic plaques. The laboratory has used bacterial products such as Gram-negative lipopolysaccharide as a model stimulus to probe the inflammatory functions of vascular wall cells for over a dozen years. This project will therefore address the specific hypothesis that components of chlamydia pneumoniae may activate inflammatory functions of vascular wall cells and leukocytes such as macrophages and lymphocytes which infiltrate atherosclerotic plaques. The pilot data suggest that **heat shock proteins** derived from the Chlamydia organism, and localized by us in many human atherosclerotic lesions, indeed elicit the production of pro-inflammatory cytokines by macrophages in vascular wall cells. This surprising finding has implications beyond atherogenesis, as **heat shock proteins** are generally considered intracellular mediators. This project will probe the mechanism of the effect of externally applied hat sock protein 60 that has been observed, and aspect of this project that should lead to new information of biological significance aside from the consideration of a role of infectious agents in cardiovascular diseases. This project will also explore the hypothesis that chlamydia pneumoniae may elicit a specific immune response in atherosclerotic mice in vivo, providing a potential novel candidate antigen for the cellular immune response now known to characterize human atherosclerosis. The investigation of the immune response to Chlamydia pneumoniae will include testing the possibility of antigenic mimicry as a possible immuno-pathogenic mechanism operating in the artery wall. This project, although new, emerges from a long standing interest of the project leader in inflammatory and immune aspects of **vascular diseases**. This project does not however contend that atherosclerosis is an infectious disease. Rather, it views infectious agents as a potential co-factor acting in concert with traditional risk factors such as dyslipidemia to potentiate atherogenesis and trigger atherosclerotic complications. The accumulating sero-epidemiological evidence and even clinical trials with antibiotics will neither establish the casual relationship between bacterial infections and atherogenesis nor elucidate the potential underlying mechanisms. The hypotheses probed in Project 1 aim to adduce new mechanistic information with implications for vascular biology and atherogenesis of general import, not limited to specific infectious processes. This project links closely with the concepts under scrutiny in Project 2. Specifically, this project will test the hypothesis that bacterial products including Chlamydia **heat shock protein** 60 can evoke or modulate aspects of the oxidative stress response in endothelial cells. The generation of the pilot data that furnishes the basis for this proposal used resources form the Vascular Pathology Core of the predecessor Program project. This project will continue to rely heavily on this Core. The focus on inflammatory mechanisms links conceptually with aspects of project 3 as well.

L60 ANSWER 89 OF 90 FEDRIP COPYRIGHT 2003 NTIS on STN
ACCESSION NUMBER: 2003:183950 FEDRIP

NUMBER OF REPORT: CRISP 5R01HL47569-12
RESEARCH TITLE: Autocrine Role of Cytokines in Vascular Smooth Muscle
STAFF: Principal Investigator: BEASLEY, DEBBIE S; DBEASLEY@LIFESPAN.ORG, NEW ENGLAND MED CTR HOSPITAL INC, 750 WASHINGTON STREET
PERFORMING ORGN: NEW ENGLAND MEDICAL CENTER HOSPITALS, BOSTON, MASSACHUSETTS
SUPPORTING ORGN: Supported By: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
PROJECT START DATE: 2002 (/01/92)
FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2011 (/30/05)
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health

SUM Recent evidence suggests that chronic infection with the respiratory pathogen, Chlamydia pneumoniae, may contribute to the development of atherosclerosis. The long range objective of this proposal is to determine the mechanisms by which infection may contribute to enhanced vascular smooth muscle cell (VSMC) proliferation, a component of early atherosclerotic lesions. The working hypothesis for these studies is that VSMC recognize and respond to cell wall components of C. pneumoniae with a strong proliferative response and upregulation of interleukin-1alpha (IL1alpha) synthesis, which in turn amplifies and sustains the initial mitogenic signal elicited by chlamydial products. Studies during the previous grant period showed that the precursor form of IL1alpha is a potent membrane-associated growth factor for human VSMC (HVSMC), and that IL1-induced proliferation involves activation of TRAF6, NIK, and IKKs, leading to the persistent activation of NF-kappaB. Preliminary data indicate that a heat-labile component of C. pneumoniae is a potent mitogenic stimulus for HVSMC. The proposed studies will determine the mechanisms of C. pneumoniae-induced HVSMC proliferation, focusing on the role of Toll-like receptor 4 (TLR4), which is expressed by HVSMC. TLRs mediate recognition of bacterial products, including lipopolysaccharide and **heat shock protein** 60, have
intracellular domains which are homologous to the type I IL1 receptor, and likewise activate TRAF6, NIK and IKKs. Two specific hypotheses will be tested in the proposed studies. First, C. pneumoniae induces HVSMC proliferation via activation of TLR4, with subsequent recruitment of TRAF6 and ultimate activation of NF-kappaB and p44/p42 mitogen-activated protein kinases. Second, autocrine production of IL1alpha, and its myristylation-dependent localization to the cell surface, sustains and enhances the primary effects of TLR4 activation. The specific aims are: to determine whether C. pneumoniae or its molecular components induce proliferation of HVSMC via TLR4- mediated activation of TRAF6, NIK, IKK, and ultimately NF-kappaB, and by TRAF6-mediated activation of p42/p44 mitogen-activated protein kinases; to determine whether autocrine production of IL1alpha precursor contributes to the mitogenic effect of C. pneumoniae in HVSMC; and to determine whether myristylation of lysine83 plays a crucial role in the mitogenic effects of IL1alpha precursor by targeting it to the plasma membrane. The studies will employ transient transfection with dominant negative mutants, TLR4 and IL1 receptor antagonists, and antisense oligonucleotides. The results of these studies will elucidate the potential roles of bacterial and chlamydial products in the pathogenesis of **vascular disease**.

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ACCESSION NUMBER: 2003:59326 FEDRIP
NUMBER OF REPORT: VA 143386
NUMBER OF CONTRACT: 0002, 644
RESEARCH TITLE: Heat Shock Protiens and Vasospasm
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PERFORMING ORGN: Department of Veterans Affairs, Medical Center, Phoenix, AZ
SUPPORTING ORGN: Supported By: Department of Veterans Affairs. Research and Development (15), 810 Vermont Ave. N.W.,

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PROJECT START DATE: Aug 30, 2001
FILE SEGMENT: Department of Veterans Affairs
SUM RELAXATION; MUSCLE, SMOOTH; CORONARY VASOSPASM OBJECTIVES 1.Characterize the interactions of HSP20 with the smooth muscle contr actile apparatus and determine the role these interactions in mediating vasorelaxation. 2.Determine the mechanisms by which phosphorylated HSP27 inhibits the phosphorylation of HSP20 and muscle relaxation. METHODOLOGY: Vasospasm contributes to the pathophysiology of numerous **vascular diseases** including, vein graft spasm during vascular reconstructive surgery or intravascular interventions, non-occlusive mesenteric ischemia, Raynaud's syndrome, and cerebral ischemia after subarachnoid hemorrhage. Our ability to effectively treat vasospastic conditions is hampered by a lack of understanding of the underlying pathophysiology and limited models of vasospasm. However, a fundamental principal of vasospasm is that the vascular smooth muscle is refractory to relaxation. We have determined that cyclic nucleotide-dependent relaxation is associated with increases in the phosphorylation of the small heat shock-related protein HSP20. We have developed a physiologic model of vasospasm, umbilical artery smooth muscle, which is uniquely refractory to relaxation and in this muscle HSP20 is not phosphorylated. Another closely related **heat shock protein**, HSP27 is highly expressed in muscle and is induced by stress. Elevated levels of phosphorylated HSP27 associated with impaired relaxation and phosphorylation of HSP20. Both HSP27 and HSP20 are actin binding proteins and may modulate smooth muscle relaxation by a direct interaction with actin or with actin associated proteins. Thus, we hypothesize that HSP20 and HSP27 co-ordinately regulate the intrinsic tone of smooth muscle and this regulation is dependent on the phosphorylation and macromolecular associations of the two small **heat shock proteins**. These studies will elucidate the molecular mechanisms of cyclic nucle otide- dependent relaxation and vasospasm due to impaired relaxation and may lead to more direct pharmacologic approaches to the treatment of vasospastic disorders. 8/16/02 Most therapeutic approaches to pathologic states that involve increased vasomotor tone such as vasospasm have targeted cell surface receptors or intracellular signaling pathways. However, we propose to identifying the mechanisms of vasorelaxation at the level of the contractile machinery where numerous signaling pathways converge. This should lead to innovative and more direct therapeutic approaches to the treatment of vasospastic disorders. PROGRESS REPORT 5/09/03: Phosphopeptide mimetics of HSP20 containing transduction domains induce relaxation of vascular smooth muscle. In addition, these mimetics induce profound changes in the actin cytoskeleton (stellation) in cultured cells. This suggests that HSP20 functions at the level of the actin cytoskeleton.

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